ACUTE ONCOLOGY INITIAL MANAGEMENT GUIDELINES

National guidelines for the initial management of adult patients, who have a cancer diagnosis, and present as an emergency or unplanned admission with a complication of their disease or cancer treatment.

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Disclaimer

The information contained in these guidelines are a consensus of the development and consultation groups' views on current treatment. They should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance process. Care has been taken in the preparation of the information contained in the guidelines. Nevertheless, any person seeking to consult the guideline, apply its recommendations or use its content is expected to use independent, personal medical and/or clinical judgment in the context of the individual clinical circumstances, or to seek out the supervision of a qualified clinician. The United Kingdom Oncology Nursing Society makes no representation or guarantee of any kind whatsoever regarding the guidelines content or its use or application and disclaim any responsibility for its use or application in any way.

Introduction

These guidelines relate to the initial assessment and immediate management of Acute Oncology patients, i.e. patients presenting with an acute problem, demonstrating symptoms deemed as having been caused by:

- Systemic Anti-Cancer Therapy (**SACT**),
- Radiotherapy,
- Malignant disease,
- A previously undiagnosed cancer where an urgent oncology/haematology assessment is required.

It is **emphasised** that these guidelines focus on initial assessment at presentation and management for the first **24 hours**. Patients should be referred to, or discussed with the Acute Oncology Team as soon as possible following presentation. The Acute Oncology team will provide further advice and on-going management guidance.

To aid in this urgent initial assessment, each protocol follows a RAG (red, amber, green) format and quick reference assessment, which is in line with the UKONS Oncology/Haematology 24-Hour Triage Tool (V2, 2016). The Common Terminology Criteria for Adverse Events (CTCAE Version 4.3) an international standard set of criteria for defining adverse events (**AE**) and their grading within clinical trials and the routine management of Oncology/Haematology patients has been applied to assist with recognition and management of Adverse Events:

http://www.hrc.govt.nz/sites/default/files/CTCAE%20manual%20-%20DMCC.pdf

Intended Audience

These guidelines are intended for use by all health care professionals who assess and/or manage acute oncology patients at presentation. The guidelines may also be useful as an adjunct to the UKONS Triage tool when providing care advice following telephone triage (Appendix 1, P.56).

They are mostly single-page "see-and-treat" guides. Whilst drug names may be referenced within each protocol, this is offered as a guide only; it is acknowledged that local variation may apply.

Please be aware of NICE National Guidelines/Pathways for the management of:

- Neutropenic Sepsis: http://pathways.nice.org.uk/pathways/neutropenic-sepsis
- Metastatic Spinal Cord Compression: http://pathways.nice.org.uk/pathways/metastatic-spinal-cord-compression.
- Metastatic malignant disease of unknown primary origin in adults: diagnosis and management: https://www.nice.org.uk/guidance/cg104

The development and consultation group worked to provide a set of generic guidelines based on national guidance and clinical expertise. They have now been reviewed and updated to ensure that they remain applicable and cover current best practice in the management of treatment induced toxicity and acute disease related complications.

The authors request that the original source is acknowledged in all copies or adaptations.

General Information and Management Principles

- **Please consider drug toxicity as a possible cause of presenting problem**. Systemic Anti - Cancer Therapy (**SACT**) includes cytotoxic chemotherapy, monoclonal antibodies, targeted agents, immunotherapy and new and novel therapies.
- **SACT toxicities can cause acute deterioration but are often reversible if managed rapidly and appropriately.** All patients on SACT may develop toxicities and are at risk; they may also have or develop additional toxicities to the one they are complaining of. Patients may be on new, novel or trial therapy, and may present with unexpected or unknown side effects.
- **Patient's should know what treatment they are receiving, and have written information about their SACT and an alert card with their 24-hour advice line telephone number.** These advice lines provide telephone triage and assessment for patients receiving treatment and will advise regarding the need for urgent assessment or review and follow up. In most cases, if a patient or carer telephones your department for advice it would be wise to redirect their call to the specialist advice line. However, if you are worried about the patient or their ability to give an accurate history, or you think that this may be a medical emergency then urgent medical review is essential.
- **If a patient sounds unwell from SACT toxicities, it is sensible to arrange oncological/haematological review or assessment in hospital.** If asking a GP or member of the primary health care team to review, it is **essential** to speak to them outlining what is required, what to look for and who to contact if further advice is needed.
- **All licensed anticancer drugs have specific toxicities and the length of time that side effects can occur following completion of treatment varies.** Most cytotoxic chemotherapies can cause side effects for up to 6 to 8 weeks after the last treatment is given. The newer immunotherapies and targeted agents can cause side effects for up to 2 years after the last treatment is administered – please ask for details and/or advice from the **acute oncology team**, the site specific specialist team, the hospital pharmacy or see the Summary of Product Characteristics: https://www.medicines.org.uk/emc/browse-medicines
- Please **see specific toxicity guideline** and manage the patient according to their condition, severity, concomitant medications and other medical problems.
- **Aggressive management (usually including HDU/ITU) is appropriate if unstable, sometimes, even in the context of advanced cancer.** Escalate care (e.g. HDU/ITU) if patient becoming haemodynamically compromised/drowsy/shut down, discuss with specialist team if unsure of appropriateness.
- **Organisations should consider using a standard triage and assessment format, such as the UKONS Triage Tool, for the assessment of patient's with cancer**. Assessment should include as standard the following questions:
- Is the patient on active treatment (including radiotherapy) at present or have they received SACT treatment in the previous 2 years?
- Names of SACT drugs and last date of treatment (NB may be on tablets)?
- Performance status, general condition, ability to carry out normal function at home? Has this changed recently? (Eastern Cooperative Oncology Group[1] or Karnofsky Performance Status[2])
- **It is important to ask about all SACT related toxicities/problems in addition to the initial complaint, as several occurring together elevate risk and need closer management.**
- **Reversible toxicities and /or problems can be treated even in the presences of any DNACPR orders, decisions should be made on an individual basis**: please discuss with acute oncology/haematology team or on call oncology/haematology consultant.

1. http://ecog-acrin.org/resources/ecog-performance-status
2. http://www.hospicepatients.org/karnofsky.html

General Information and Management Principles - continued

- **Neutropenia can occur:**
    - **At any time during a course of certain SACT or up to 6 weeks after**
    - **With certain radiotherapy treatment**
    - **At any time in a patient with disease-related immunosuppression**

Patient's with a suspected neutropenic sepsis will require IV antibiotics within 1 hour of presentation for assessment.

- **Review concomitant medications and consider stopping** those that may affect renal function/ potentiate hypotension (e.g. ACE-inhibitors, diuretics) if unwell or hypotensive and benefits outweigh the risks of doing so.
- **Establish intravenous access**, or utilise indwelling lines if appropriately trained to do so, and hydrate according to clinical condition. Monitor fluid balance closely.
- **Patient's require daily medical review and daily bloods may also be required** (watch for neutropenic sepsis/ dehydration). **Be aware that administering paracetamol/antipyretics to neutropenic patients may mask signs of sepsis.**
- **Rectal examination.** Due to the risk of damage to rectal mucosa, it is recommended that in patients receiving SACT rectal examination is not performed. If it is deemed necessary to conduct rectal examination, this should be undertaken with caution.
- **The patient's site-specific specialist team providing cancer treatment must be informed** of any admission/assessment, as adjustments to the subsequent cycle may be required. If patient is in a clinical trial, the trials team should be contacted about the admission.
- **Consider the involvement of the palliative care team** for symptom control advice if the problem is disease related.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 1. ANAPHYLAXIS/ALLERGIC REACTION/HYPERSENSITIVITY Requires IMMEDIATE medical assessment!

Hypersensitivity or an allergic reaction is an inappropriate and excessive reaction to an allergen; severity ranges from mild allergy to severe systemic reactions leading to anaphylactic shock if left untreated.

Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction. It is characterised by rapidly developing, life-threatening problems involving: the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia). In most cases, there are associated skin and mucosal changes.

Treat as an emergency according to Resuscitation Council Anaphylaxis Guidelines.

https://www.resus.org.uk/anaphylaxis/emergency-treatment-of-anaphylactic-reactions/

Signs and symptoms:

Bronchospasm	Cough	Dizziness	Dyspnoea
Headache	Hypertension	Hypotension	Nausea, vomiting
Urticaria	Tachycardia	Rigors/chills	Pruritus/itching
Arthralgia	Myalgia	Asthenia	Rash
Swelling of tongue/throat			

Assessment: **ABCDE** approach **Observations:** Calculate and monitor NEWS score. ECG Cardiac monitoring

Questions: What treatment/drug is the patient receiving? Any known allergies?
Cancer diagnosis/primary disease? Concurrent medications?

Differential diagnosis includes: infusion reaction; cytokine release syndrome, asthma, septic shock, and transfusion reaction

If this occurs during administration of treatment **-STOP infusion/transfusion immediately**

Grade 1 (Green)
Mild transient reaction: intervention or infusion interruption not required.

Grade 2 (Amber)
Intervention or infusion interruption indicated; all symptoms respond promptly to treatment (E.g. antihistamines; NSAIDS, IV Fluids).

Grade 3 (Red)
Prolonged signs and symptoms **not** rapidly responsive to medication and/or brief interruption of infusion or **recurrence** of symptoms following initial improvement

Grade 4 (Red)
Anaphylaxis – Airway, **B**reathing, **C**irculation problem -Life threatening consequences; urgent intervention required.

- Treat reaction in line with local guidelines/policy.
- Prophylactic medications indicated for 24 hours.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

Treat as an emergency according to Resuscitation Council Anaphylaxis Guidelines – Page 7.

- Patients who have had a suspected anaphylactic reaction should be treated and observed for at least 6 hours in a clinical area with facilities for treating ABC problems[1]
- Patient should be reviewed by a senior clinician and a decision made about the need for further treatment or a longer period of observation
- Manage in accordance with trust local guidelines depending upon differential diagnosis.
- Check that the patient is not neutropenic –if sepsis suspected manage accordingly

Patients with a good response to initial treatment should be warned about recurrence of symptoms and in some circumstances be kept under observation for 24 hours.
This includes the following:

- Severe reactions with slow onset
- Individuals with severe asthma or a severe asthmatic component
- Patients with a history of biphasic reactions

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

https://www.nice.org.uk/guidance/cg134/evidence/anaphylaxis-full-guideline-pdf-184946941

Resuscitation Council (UK)

Anaphylactic reaction?

Airway, Breathing, Circulation, Disability, Exposure

Diagnosis - look for:
- Acute onset of illness
- Life-threatening Airway and/or Breathing and/or Circulation problems [1]
- And usually skin changes

- **Call for help**
- Lie patient flat
- Raise patient's legs

Adrenaline [2]

When skills and equipment available:
- Establish airway
- High flow oxygen
- IV fluid challenge [3]
- Chlorphenamine [4]
- Hydrocortisone [5]

Monitor:
- Pulse oximetry
- ECG
- Blood pressure

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1 Life-threatening problems:

Airway:	swelling, hoarseness, stridor
Breathing:	rapid breathing, wheeze, fatigue, cyanosis, SpO_2 < 92%, confusion
Circulation:	pale, clammy, low blood pressure, faintness, drowsy/coma

2 Adrenaline *(give IM unless experienced with IV adrenaline)*
IM doses of 1:1000 adrenaline (repeat after 5 min if no better)

• Adult	500 micrograms IM (0.5 mL)
• Child more than 12 years:	500 micrograms IM (0.5 mL)
• Child 6 -12 years:	300 micrograms IM (0.3 mL)
• Child less than 6 years:	150 micrograms IM (0.15 mL)

Adrenaline IV to be given **only by experienced specialists**
Titrate: Adults 50 micrograms; Children 1 microgram/kg

3 IV fluid challenge:
Adult - 500 – 1000 mL
Child - crystalloid 20 mL/kg

Stop IV colloid
if this might be the cause
of anaphylaxis

	4 Chlorphenamine (IM or slow IV)	**5 Hydrocortisone** (IM or slow IV)
Adult or child more than 12 years	10 mg	200 mg
Child 6 - 12 years	5 mg	100 mg
Child 6 months to 6 years	2.5 mg	50 mg
Child less than 6 months	250 micrograms/kg	25 mg

Guideline 2. ARTHRALGIA/MYALGIA Initial triage assessment within15 minutes

Normally a symmetrical widespread joint pain but can also be associated with muscle pain (myalgia).
Certain drugs can cause arthralgia, including: Taxanes, BRAF inhibitors, GCSF, Immunotherapies.

Identify: patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant, they may be myelosuppressed/ neutropenic and at risk of sepsis. If present, this should be managed according to guidelines.

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&E and Ca^{2+}.

For patients receiving or received **immunotherapy** consider:

- Endocrine function panel -TSH, Free T4, Free T3, ACTH, LH, FSH and Cortisol, Prolactin, Blood Glucose, +/- Testosterone/Oestrogen and refer to endocrinopathy guidelines on pages 27 to 36
- CK and ESR to rule out Autoimmune Arthritis/Myositis

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Has the patient taken anything for pain?
- Where is the pain? (If not widespread then consider other causes of joint pain e.g. localised pain in isolated joint/back/spine may be related to metastatic deposit and need investigation and discussion)
- How long has the patient had the pain? Is the pain affecting what they can do?
- Has/is the patient receiving GCSF, filgrastim/pegfilgrastim injections? Some patients receiving GCSF may experience severe muscle pain commonly in the pelvic area, lower back and/or shoulders, which will usually improve after stopping GCSF. When was the last injection?
- Are there any comorbidities that may cause arthralgia/myalgia e.g. autoimmune Rheumatoid Arthritis or Systemic Lupus Erythaematosis
- Is the patient on any blood thinning drugs or steroids?

Grade 1(Green)
Mild Pain - not interfering with daily activities

- Reassure the patient that this is normal, generally nothing to worry about and associated with treatment.
- Advise to observe temperature closely - if patient develops temperature they must phone helpline immediately for advice.
- Review current analgesia and consider paracetamol, non steroidal (with caution as may not then develop a temperature in response to infection) or opiate if pain severity merits it
- Heat - a heat pad, covered hot water bottle or regular warm baths. Advise patient to get plenty of rest and plan activities to include rest periods
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

Grade 2(Amber)
Moderate pain - Interfering with some normal activities

Grade 3(Red)
Severe pain – and /or loss of ability to perform some activities

- Advice and support measures as Grade 1& 2.
- You must check that the patient is not neutropenic if discharge home is being considered
- Review analgesia – consider codeine or opiate based or non steroidal if not contraindicated, or neuropathic agent if appropriate
- Advise to observe temperature closely - if patient develops an abnormal temperature they must phone immediately for advice.

Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

Grade 4(Red)
Bedridden or disabling

- Arrange urgent admission for on going assessment and treatment.
- Ensure the patient is not neutropenic.
- Review analgesia – consider codeine or opiate based or non steroidal if not contraindicated, or neuropathic agent if appropriate
- Seek specialist oncology advice if pain is not settling.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 3. BLEEDING AND/OR BRUISING - Requires IMMEDIATE medical assessment.

Bleeding can occur secondary to injury, disease, or as a side effect of treatment. It can be a life-threatening event if massive blood loss or spontaneous bleeding occurs.

Thrombocytopenia – is a reduction in the number of platelets in the blood. If platelet count is < 50 bleeding and or bruising may occur with minor trauma.

Intracranial haemorrhage is more likely if there is **sepsis** and a platelet count of < 20

In a **non-septic** patient a platelet count of 10 or above may be adequate in the absence of additional risk factors for bleeding

Coagulation abnormalities – due to disease e.g. liver metastases or disseminated intravascular coagulation (DIC) or treatment e.g. anti-coagulation therapy.

Identify: patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant, they may be myelosuppressed / neutropenic and at risk of sepsis. If present, manage accordingly.

Many haematological disorders (malignant and non-malignant) can cause thrombocytopenia. Some patients, e.g. those with chronic lymphocytic leukaemia (CLL) or lymphoma may develop idiopathic thrombocytopenic purpura (ITP).

Patients who are receiving certain systemic anti-cancer treatment are at risk of thrombocytopaenia

If present, these conditions should be managed according to approved guidelines.

Observations: Calculate and monitor NEWS score.

Investigations: Urgent FBC, U&E, LFTs. Consider group and cross match. Coagulation screen. INR (if on Warfarin). APTT ratio (if on IV Heparin). Anti-Xa level if on low molecular weight (LMW) heparin, as it can accumulate in the presence of renal failure. Fibrinogen if considering DIC.

Examination: Associated symptoms: Light headed, pallor, clammy, thirst, rash (petechial/purpura/ punctate)

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Is the patient actively bleeding? Site of active bleeding? Injury related or spontaneous?
- How much blood has the patient lost?
- Onset and duration – when did bleeding and/or bruising start and how long has it persisted?
- Have they had similar bleeding and /or bruising before?
- Allergies/ current medications? - Anticoagulants, aspirin, clopidogrel, NSAIDS, DOACs (new anticoagulants e.g. rivaroxaban /apixaban) - **NB** Heparin can cause thrombocytopaenia.
- Relieving factors – Is it stopped via direct pressure or other measures?

Grade 1 (Amber)
Bleeding - mild self limiting, controlled by conservative measures, ecchymosis, occult blood in secretions
Bruising - petechiae or bruising in a localised or dependant area, with or without trauma.

- Review blood results
- Manage neutropenia as per guideline **12** on **P.19-20**
- Discuss abnormalities with on call haematologist or oncologist
- Do not discharge a patient without prior discussion with on call haemato-oncolologist or oncologist
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

Grade 2 (Red)
Bleeding - loss of 1-2 units
Bruising - moderate petechiae, purpura and/or generalised bruising, with or without trauma.

Grade 3 (Red)
Bleeding - loss of 3-4 units.
Bruising - generalised petechiae, purpura and/or bruising.
New bruises, without significant trauma.

Grade 4 (Red)
Massive bleeding loss of > 4 units.
Life threatening haemorrhage.

- Manage according to emergency department resuscitation guidelines
- Attention should be given to disease or treatment specific factors e.g. thrombocytopenia, advanced disease.
- Consider stopping any contributing medication if safe to do so e.g. anti-coagulants /NSAIDS/antiplatelet drugs – discuss reversal of anti-coagulants with haematology
- All patients should be discussed with on call haemato-oncolologist and/or oncologist, who can provide further management advice
- Admit for support and monitoring - Consider critical care management
- Manage neutropenia as per guideline **12** on **P.19-20**

Always make sure that the Acute Oncology Team are informed of the patient's assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 4. CHEST PAIN Requires IMMEDIATE medical assessment

Pain may result from a wide range of causes, there is an urgent need to diagnose the cause of any patient presenting with chest pain to ensure that serious and life-threatening conditions are not missed.

Identify: Patients within 6/52 of chemotherapy specifically patients currently receiving 5 fluorouracil (5FU) or capecitabine, which can cause coronary artery spasm. Patients may be taking these drugs orally at home or via continuous infusion. Other chemotherapy drugs/monoclonal antibodies can cause reduction in heart function but this is not usually an acute presentation.
All cancer patients have an increased risk of pulmonary embolism.
Observations: Calculate and monitor NEWS score.
Investigations: Urgent FBC, U&E, Cardiac markers. Urgent ECG. Consider ABGs, CTPA.
Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient currently receiving 5FU/capecitabine?
- Does the patient have a history of angina, or other heart disease?
- Exacerbating / relieving factors, and characteristics of pain?
- Associated symptoms, e.g. SOB, syncope, oedema, palpitations
- Consider is this pain cardiac? Differentials for chest pain in oncology/haematology patients include cardiac cause, pulmonary embolism (PE), indigestion, disease progression or metastases

Advise Urgent A&E assessment for all symptoms of chest pain

Action: Treat chest pain as 'Red' until proven to be non-cardiac/life threatening

The aim is to exclude a life-threatening cause, which needs immediate treatment, from other causes of chest pain.
! If PE strongly suspected and same day CTPA not possible, consider commencing treatment with LMWH pending definitive investigation/diagnosis

! Is the patient connected to an ambulatory intravenous infusion pump of 5 fluorouracil (SACT)? – If so arrange urgent disconnection.

! Is the patient taking oral SACT such as capecitabine? - If so ensure patient does not continue with this medication

! These patients may also be myelosuppressed/ neutropenic and at risk of sepsis. If present, this should be managed according to approved guidelines

- Admit for monitoring and on going assessment and management in accordance with local trust guidelines.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 5. CONSTIPATION Initial triage assessment within 15 minutes

Irregular and infrequent or difficult evacuation of the bowels; can be a symptom of intestinal obstruction or diverticulitis.

Identify: Patients who have received/receiving SACT or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20

Observations: Calculate NEWS score. Presence of bowel sounds.

Investigations: Urgent FBC, U&E, CRP, Ca^{2+}, and LFTs. Consider abdominal X-ray.

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- When did the patient's bowels/stoma move last? Are they passing wind?
- What is normal bowel habit? Any recent changes? N.B. loose runny stools could be overflow.
- What medication are they taking and has there been any recent changes? Certain medication can cause constipation e.g. anti-emetics (5HT3 Antagonists), opioids, SACT including vinca-alkaloids
- What food and fluids have they been taking over last few days? Decreased fluid and/or food intake can be significant factors in constipation
- Is there any nausea or vomiting?
- Is there any abdominal pain? Is it getting worse
- Are they passing water/urine normally?

Examination: PR Examination (with caution in haematology patients). Presence and nature of bowel sounds. Rule out signs and symptoms of bowel obstruction.

N.B. constipation may be a presenting symptom of MSCC or hypercalcaemia. Ascites can often aggravate constipation – if present consider drainage.

Differential diagnosis includes: Drug related e.g. SACT, opiates, anti-emetics. Bowel obstruction/ileus secondary to disease or ascites. Hypercalcaemia.

Grade 1 (Green)
Mild-no bowel movement for 24 hours over pre-treatment normal

Grade 2 (Amber)
Moderate- no bowel movement for 48 hours over pre-treatment normal

Grade 3 (Red)
Severe- no bowel movement for 72 hours over pre-treatment normal

Grade 4 (Red)
No bowel movement for > 96 hours -consider paralytic ileus or bowel obstruction

ACTION: Grade 1 and Grade 2

- Dietary advice including good fluid intake
- Stop or change constipating drugs
- Consider use of laxatives, faecal softener or stimulant
- If patient is discharged they should be encouraged to make contact if symptoms persist or worsen.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

- Review medication and stop/ change /avoid constipating drugs e.g. opiates, certain anti- emetics
- Dietary advice including good fluid intake
- Consider admission for investigation and management if associated with: -
  - *Abdominal pain
  - *Nausea/vomiting
- Consider nil by mouth instructions and arrange surgical review if indicated.

Patients may also have:

- Severe abdominal pain and/or distension
- Nausea and Vomiting
- Faecal smelling vomit
- Rigid abdominal distension
- History of abdominal Surgery

Admit for: -

- Further management and investigation
- Senior medical and/or surgical review
- I.V. access and fluid replacement
- Consider nil by mouth instructions and naso- gastric tube placement
- Analgesia
- Emesis control
- Monitoring

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 6. DIARRHOEA (2 page guideline). Initial triage assessment within 15 minutes

A disorder characterised by frequent and watery bowel movements. Grading is relative to normal baseline function.

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20

Observations: Calculate and monitor NEWS score.

Investigations: Urgent FBC, U&E + magnesium, LFTs, CRP, abdominal X-ray.

Stool sample for C&S/ova/cysts/parasites to rule out infective causes of diarrhoea-e.g. Campylobacter/salmonella and CDT screen.

Do NOT assume this is infective it is most likely to be drug induced in this group of patients

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Is the patient receiving radiotherapy to the abdomen or pelvis and when was their last treatment?
- How many stools a day above normal amount? or how much stoma output is there above normal amount? Have they had any nocturnal movements? For how many days have they had diarrhoea? Is it interfering with activities of daily living?
- Are stools/stoma outputs formed, loose or watery? Any faecal incontinence or urgency? Any blood or mucous in the stool?
- Is there any abdominal pain e.g., cramping pains coming in waves?
- Is the patient able to eat and drink normally? Are they passing plenty of clear urine?
- Does the patient have any other SACT related toxicities, e.g. mouth ulcers, mucositis, nausea/vomiting, red hands/feet?
- Has the patient taken any antibiotics recently or been in hospital recently?
- What medication have they taken? Have they taken any laxatives or anti-sickness medication **or** any anti-diarrhoeal medication in the last 24 hours? If so what?

Differential diagnosis includes:

- **Graft versus host disease** in stem transplant patients – contact transplant haematologist **urgently**
- **Secondary to SACT e.g.** 5FU or CAPECITABINE, IRINOTECAN, any TKI, please see next page and specific **DRUG INFORMATION SHEET** for further management guidance. **Consider DPD deficiency**
- **Gastrointestinal symptoms due to IMMUNOTHERAPY - proceed to guideline 21 on page 30 for further guidance**
- **Infection**
- **Constipation** with overflow
- **Radiotherapy –** secondary to treatment

Grade 1 Amber
Increase up to 3 bowel movements a day over pre-treatment baseline or mild increase in ostomy output

Grade 2 (Amber)
Increase up to 4-6 episodes a day over baseline or moderate increase in ostomy output or nocturnal movement or moderate cramping

Grade 3 (Red)
Increase up to 7-9 episodes a day or severe increase in ostomy output
* and/or incontinence * and/or severe cramping
* and/or bloody diarrhoea

Grade 4 (Red)
Increase > 10 episodes a day or grossly bloody diarrhoea

Review medication WITHHOLD DRUGS including any SACT that may be contributing until Acute Oncology or Site Specific team review

ESCALATE TO RED for any of the following:

- **Grade 2 and receiving or received immunotherapy treatment in the last 12 months**
- **Grade 2 for >24 hours despite anti-diarrhoeal medication**
- **Other symptoms e.g. temperature, nausea/vomiting, mouth ulcers, or clinical concerns**
- **Haematology patient**
- **Oncology -** Consider loperamide initially. If ineffective consider Codeine Phosphate. Reduce and then stop antidiarrheal after 12-24 hours free of diarrhoea.
- Review any other SACT toxicities according to guidelines.
- Review all medications and stop prokinetics and laxatives once constipation with overflow has been ruled out. Avoid domperidone and metoclopramide anti-emetics.

Patients with grade 3 or 4 diarrhoea require specialist secondary care to manage symptoms -_IV resuscitation may be required. They should be admitted further assessment and active management.
WITHHOLD SACT until Acute Oncology Team review and review all other medication as they may be contributing – if receiving Capecitabine or 5FU consider DPD deficiency
If receiving or received immunotherapy treatment in the last 12 months - follow guideline 21 on page 30
Haematology patients – discuss with haematology team, urgently.
Further management detail on the page 13.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 6 continued. **DIARRHOEA**

Initial Management

1. Consider infective diarrhoea:

Isolate until infection excluded

- Send stool sample urgently - Inform microbiology and discuss management with microbiologist
- If haematology patient or strong suspicion of infective diarrhoea, withhold anti-diarrhoeal medication until stool result available
- Give antibiotics according to local policy (e.g. for C.Difficile or neutropenic sepsis) **Consider** administering antibiotics empirically if not settling.

2. Consider graft versus host disease in stem transplant patients – contact transplant haematologist **urgently**

3. Secondary to SACT e.g. 5FU or CAPECITABINE, IRINOTECAN, ERLOTINIB any TKI or Targeted Therapy please see specific **DRUG INFORMATION SHEET** for specific management guidance.

4. **Gastrointestinal symptoms due to IMMUNOTHERAPY** **-** proceed to guideline 21 on page 30 for further guidance

5. Neutropenic Sepsis – if there is suspicion of, or potential for neutropenic sepsis start antibiotic management immediately as per policy (guideline 12 on pages 19-20) – do **not wait for FBC.**

6. IV fluid resuscitation. Replace fluid and electrolyte losses. Adjust on-going fluids according to fluid balance status and renal function.

7. Full medication review - **Stop** ACE-inhibitors/ diuretics/ NSAIDs. NB Folic Acid can potentiate and increase side effects of some SACT drugs

8. Nil by mouth (except sips) if abdominal pain or distension or abnormal abdominal X-ray

9. Antidiarrhoeal -

- **Haematology -** Discuss with haematology team on call before commencing antidiarrhoeal

- **Oncology:**
  - Consider loperamide 4mg initially then 2mg after each loose stool (maximum16mg per 24 hours) **N.B. Caution with high doses or prolonged use of loperamide as it can cause paralytic ileus**
  - If loperamide ineffective, then consider codeine phosphate instead of or in addition
  - Reduce/stop antidiarrhoeal after 12-24 hours free of diarrhoea.
  - If Grade 4 – consider the use of octreotide by sc injection and immediate IV broad-spectrum antibiotic (even if afebrile). Withhold if not on maximal antidiarrhoeal prior to admission but review every 24 hours.
  - Do not withhold antidiarrhoeal for more than 12-24 hours without thorough senior medical review.

10. Consider hyoscine butylbromide if abdominal spasms

Guideline 7. DYSPNOEA/SHORTNESS OF BREATH. Requires IMMEDIATE medical assessment.

Difficulty breathing may include symptoms such as wheezing, choking, and a feeling of not getting enough air into lungs. Dyspnoea indicates a conscious appreciation of increased work done during breathing; principal factors in SOB are an increased work of breathing, increased ventilatory drive, impaired muscle function.

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed/neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&E, Sputum C&S, blood cultures and CRP if pyrexial. ECG and CXR. Risk assess for VTE. Consider ABGs and troponin. Consider CTPA/VQ investigations to rule out pulmonary embolism, pneumonitis. Consider D-dimer.

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Cardinal questions related to breathlessness including history of underlying chest complaint, asthma, COPD, ischaemic heart disease
- Is there any chest pain?
- What is the patients current medication?
- Is there a history of dyspnoea? What is their normal level? Is this a new symptom?
- Are there any exacerbating/relieving factors?
- Is there any pain or swelling in legs? – assess for signs of DVT

Differential diagnosis includes:

Chest Infection	Disease progression	New cancer diagnosis or metastases	Pleural effusion
Pulmonary embolism (PE)	Consolidation	Superior vena cava obstruction (SVCO)	Cardiac ischaemia
Anaemia	Pneumonitis	Exacerbation of respiratory condition e.g. Asthma	Lymphangitis

Grade 1 (Amber)
New onset dyspnoea with moderate exertion

- Assess for signs of sepsis: such as productive cough, pyrexia, generally unwell (Escalate to Red as appropriate)
- Anaemia – consider correction
- A history of underlying chest complaints e.g. asthma, COPD: advise patients around usual management of exacerbations and advise to discuss with GP or health professional managing this condition
  - You must check that the patient is not neutropenic prior to discharge
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

Grade 2 (Red)
New onset dyspnoea with minimal exertion

Grade 3 (Red)
New onset dyspnoea at rest

Grade 4 (Red)
Life threatening symptoms requiring ventilatory support

- Ensure the patient is not neutropenic – **If present, this should be managed as per guideline 12 on P.19-20** - immediate antibiotics if sepsis suspected
- Admit if evidence of:

- Desaturation
- Infection
- Other chemotherapy toxicities

For management of;

- **SVCO** - see guideline 40 on P.51
- **Pleural effusion** - see guideline 37 on P.48
- **Carcinomatous Lymphangitis** – see guideline 29 on P.38
- **Pneumonitis** may be drug or radiation related:
  - **Radiation pneumonitis** - see guideline 39 on P.50
  - **Immunotherapy** induced pneumonitis – see guideline 24 on P.33
- Discuss with Acute Oncology Team
- Manage all other causes in accordance with trust local guidelines depending upon differential diagnosis:
- https://www.brit-thoracic.org.uk/standards-of-care/guidelines/btssign-british-guideline-on-the-management-of-asthma/
- COPD - https://www.nice.org.uk/guidance/CG101

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 8. FATIGUE Initial triage assessment within 15 minutes

Fatigue is a subjective unpleasant symptom, which incorporates total body feelings ranging from tiredness not relieved by rest or sleep to total exhaustion creating an unrelenting overall condition that interferes with the individual ability to function to their normal

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&E, group and save, CRP, blood glucose, consider blood cultures, Ca^{2+}, If the patient is receiving or has received **immunotherapy** in the past 12 months, check random cortisol, TSH, T4, T3.

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- How many days have they been feeling like this?
- Do they have any pain? Have they taken any painkillers? If so, what?
- Are they able to eat and/or drink?
- Are they short of breath?
- Are they able to mobilise – ambulant – performance status?
- Are they passing usual amounts of urine and are bowels functioning normally?
- Patient mood? Has thier mood changed recently? Are they receiving any psychological support?

Differential diagnosis includes:

- Anaemia
- Side effect of treatment
- Immunotherapy induced endocrinopathy
- Hormone disturbance e.g. thyroid dysfunction
- Disease progression
- Patient entering the dying phase
- Depression/psychological problems

Grade 1 (Green)
Increased fatigue but not affecting normal level of activity

Grade 2 (Amber)
Moderate or interfering with some normal activities

- Check all blood results prior to discharge and escalate any abnormalities:
  - Neutropenia/pancytopenia
  - Endocrine disturbance in immunotherapy
- Advice:
  - Encourage diet and fluids
  - Regular exercise

  Consider psychological support measures
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

Grade 3 (Amber)
Severe or loss of ability to perform some activities

- Check all blood results and escalate any abnormalities:
  - Neutropenia/pancytopenia
  - Endocrine disturbance in immunotherapy
- Escalate if evidence of:
  - Dehydration
  - Infection
  - Poor oral intake
  - SACT toxicities
- Consider possible disease progression.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

Grade 4 (Red)
Bedridden or disabling

- Check all blood results and act on abnormalities e.g.
  - Neutropenia/pancytopenia *guideline 12 P.19-20
  - Endocrine disturbance in immunotherapy *guidelines 18,19,20 on Pages .27, 28,29.
- Admit for:
- Monitoring and continued assessment
- Management according to symptoms/blood results.
- Contact the acute oncology team for advice on continuing anti-cancer therapy and consider possible disease progression.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 9. METASTATIC SPINAL CORD COMPRESSION (MSCC)/ Cauda Equina Syndrome.
IMMEDIATE medical assessment.

MSCC is due to a pathological vertebral body collapse or direct tumour growth causing compression of the spinal cord. Irreversible neurological damage ensues with resulting paraplegia. Early diagnosis and treatment is essential.

Identify:

- **Patients with known diagnosis/history of, or suspected cancer. Please note to rule out spinal cord compression, MRI scan must be performed within 24 hours of clinical suspicion.**
- **Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and are at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20** - immediate antibiotics if sepsis suspected.
- **Observations:** Calculate and monitor NEWS score. **Examination:** Full neurological assessment and on-going review
- **Investigations: Urgent MRI whole spine within 24 hours of clinical suspicion.** Urgent FBC, U&E, LFT, Group & Save, Ca^{2+}. If considering myeloma/plasmacytoma then Immunoglobulins/electrophoresis, serum light chains and urine bence jones protein. If considering lymphoma then LDH. If new diagnosis of cancer consider appropriate tumour markers to aid diagnosis.

Key signs/symptoms:

- The patient may or may not have a cancer diagnosis/primary disease
- Referred back pain that is multi segmental or band like
- Escalating pain which is poorly responsive to treatment, including medication
- Different character or site to previous symptoms
- Funny feeling, odd sensations or heavy legs (multi segmental), pins and needles
- Lying flat increases back pain
- Pain, worsening on coughing or sneezing
- Agonising pain causing anguish and despair
- Gait disturbance, unsteadiness, especially on stairs (not just limp)
- Sleep grossly disturbed due to pain being worse at night
- Established motor/sensory/bladder / bowel disturbances incontinence are late signs

If you have suspicion of MSCC then contact the Acute Oncology team and/or MSCC coordinator for advice regarding management

Grade 1 (Amber)
Mild paraesthesia, subjective weakness; no objective findings

- Rule out spinal cord compression – full neurological examination
- Discuss with the Acute Oncology Team and/or MSCC Coordinator
- MRI whole spine to be performed within 1 week of clinical suspicion
- Advise on pain control
- **DO NOT** discharge the patient until you are sure they do not have MSCC.
- If you do discharge the patient:
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen/persist.

Grade 2 (Red)
Mild or moderate sensory loss, moderate paraesthesia, mild weakness with no loss of function

Grade 3 (Red)
Severe sensory loss, paraesthesia or weakness that interferes with function

Grade 4 (Red)
Paralysis

- Rule out spinal cord compression/cauda equine - Urgent MRI whole spine
- Treat as unstable spine until MRI results reported or oncology/neurosurgical assessment
- Admit for monitoring and on going assessment
- Commence:
  - Dexamethasone 16mg stat dose followed by16mg daily
  - Analgesia
  - Thromboprophylaxis

N.B. **Note:** need for caution in patients with no previous known malignancy and lymphoma suspected steroids might cause rapid resolution of the tumour, which may make histological diagnosis very difficult. If possible, steroids should be avoided before biopsy if lymphoma suspected.

- Contact MSCC coordinator or oncologist on call to assess and plan treatment – radiotherapy or surgery-if required
- All patients should start definitive treatment within 24 hours once MRI confirms a diagnosis of MSCC.
- See your trust/network agreed algorithm for more detailed local guidance including contact details for the specialist team.
- Please consider Cancer of Unknown Primary (CUP), guideline 38 for patients who present with metastatic disease **without** a previous diagnosis of cancer

For further information see NICE Metastatic Spinal Cord Compression guideline at http://pathways.nice.org.uk/pathways/metastatic-spinal-cord-compression#

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline10. MUCOSITIS/STOMATITIS/OESOPHAGITIS Time to initial assessment - 15 minutes

An inflammatory reaction of the mucous lining of, the upper gastrointestinal tract from mouth to stomach (mouth, lips, throat), and surrounding soft tissues.

Identify: Patients who have received/receiving SACT or are at risk of disease related immunosuppression or a history of stem cell transplant (PBSCT). These patients may be myelosuppressed /neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected.

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&Es, LFTs, CRP, Lactate and Blood Cultures (Oncology patients - consider the need for pathology investigations in grade 1 and 2 presentations on an individual basis and in light of any other presenting symptoms or risk factors)

Examination and questions:

- Is there a cancer diagnosis/primary disease?
- Is this a haematology patient? If so please contact haematology team as soon as possible.
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Is there evidence of super added infection? Does the patient have any blisters, ulcers or white patches on tongue/ lips mouth?
- Is there any pain or bleeding from the mouth?
- Are they able to eat and/or drink?
- Does eating or swallowing make the pain worse?
- Are they using any mouthwashes, painkillers or other treatments within the mouth?
- Do they also have diarrhoea?
- Is there any dryness, pain, inflammation of genitals and/or rectum – consider rectal mucositis
- Are they passing usual amounts of urine?
- Have they had any recent radiotherapy treatment to the head and/or neck?

Differential diagnosis includes:

- Radiotherapy reaction
- SACT related
- Viral/bacterial infection
- Candidiasis

Grade 1 (Green)
Painless ulcers, erythema or mild soreness, able to eat and drink normally

Grade 2 (Amber)
Painful ulcers and /or erythema, mild soreness but able to eat and drink normally

Grade 3 (Red)
Painful erythema, and difficulty with eating and drinking

Grade 4 (Red)
Significant pain, minimal intake and /or reduced urinary output

Consider the following mouth care advice:

- Ice chips for symptomatic relief
- If painful: an anti-inflammatory mouthwash
- Consider the use of a mucosal barrier gel
- Analgesia: use care if advising antipyretic as it may mask signs of neutropenic sepsis
- Assess for thrush/candidiasis and arrange for an antifungal agent to be prescribed if required
- You must check that the patient is not neutropenic prior to discharge
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

- Check all blood results and act on abnormalities e.g. Neutropenia or pancytopenia
- Assess for evidence of:
  - Dehydration
  - Infection
  - Poor oral intake
  - Other SACT toxicities
- If receiving Capecitabine or 5FU consider DPD deficiency
- Admit for monitoring and management
- Consider parenteral hydration
- Analgesia, consider:
  - Dispersible analgesics e.g. soluble paracetamol /co codamol
  - If no improvement consider opiates
- Assess for thrush/ candidiasis and arrange for an antifungal agent to be prescribed if required
- Consider referral to the SALT team and dietician for management support
- Consider the following mouth care advice:
  - Ice chips for symptomatic relief
  - If painful: anti-inflammatory mouthwash
  - Consider the use of a mucosal barrier gel

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 11. **NAUSEA** **Initial triage assessment within 15 minutes**

Nausea is the sensation of being about to vomit. Acute chemotherapy induced nausea usually presents within the first 24 hours of receiving treatment. Delayed nausea may present any time after the first 24 hours and continues for up to 6 or 7 days after treatment

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected.

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&Es, LFTs, Ca^{2+}, blood cultures and CRP, (consider the need for pathology investigations in grade 1 and 2 presentations on an individual basis and in light of any other presenting symptoms or risk factors)

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- How often are they feeling sick/nauseous?
- Have they been sick/vomited?
- Assess bowel movements, any symptoms that suggest constipation? Any diarrhoea? Bowel obstruction?
- What food and fluids have they been taking over last few days?
- Any evidence of reflux/gastritis?
- Any signs of dehydration e.g. decreased urine output, fever, thirst, dry mucous membranes etc.
- What is the extent of the disease? – e.g. known metastases to brain, bone, liver etc.
- Are they taking any medication and has there been any recent change?
- Are they currently receiving radiotherapy? (Especially to brain, liver, GI Tract)
- Do they have any abdominal pain? Is this a new symptom?

Differential diagnosis includes:

- Medication related e.g. SACT
- Gastric stasis
- Hypercalcaemia
- CNS disease
- Gastro intestinal infection
- Disease related

Grade 1 (Green)
Able to eat and drink with a reasonable intake

Grade 2 (Amber)
Able to eat and drink but intake is significantly reduced

Grade 3 - 4 (Red)
Inadequate or no oral caloric and/or fluid intake

- Review prescribed antiemetic medication make sure dose / route and frequency are appropriate and assess patient compliance and understanding
- Fully investigate cause:
  - Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - Medication related e.g.SACT, opiates etc.
- When cause has been clearly identified, change antiemetic in line with local policy directions
- Advise self help measures:

https://www.macmillan.org.uk/information-and-support/coping/side-effects-and-symptoms/other-side-effects/nausea-and-vomiting.html#290074

- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

- Admit for further assessment and management.
- IV fluids and electrolyte replacement as appropriate
- Fully investigate cause:
  - Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - Medication related e.g.SACT, opiates etc.
- Prescribe antiemetic as appropriate to cause in line with local policy
- Consider alternative route of administration of antiemetic's e.g. syringe driver especially if associated with vomiting

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 12. (2-page guideline) **Suspected Neutropenic Sepsis** **IMMEDIATE assessment**

Clinical suspicion of infection and potential for neutrophils <0.5x10⁹L (NICE)

(Patients who have received or receiving SACT or have a history of myelosuppression or known bone marrow failure have the potential for neutropenia)

Initial assessment:

- Identify patients with clinical suspicion of infection and potential for neutrophils <0.5 x10⁹L (received or receiving SACT or history of myelosuppression or known bone marrow failure)
- Patients may appear well initially but if untreated can rapidly progress to septic shock + death. Early diagnosis will normally prevent death.

START TREATMENT AT POINT OF SUSPICION

Immediately: Take bloods and administer 1st IV antibiotics (DON'T wait for FBC result)

Door to needle time for first antibiotics should be less than one hour.

- **Urgent:** FBC, U&Es, LFT's include albumin, Coagulation screen, G+S, Ca^{2+}, PO^{4-}, Mg^{2+}, Urate, CRP, and Lactate peripheral and central line blood cultures
- **Observations:** Calculate NEWS score. Assess urine output
- **Commence:** NEWS chart – patients can deteriorate rapidly and should be monitored closely. Monitor urine output.

Clinical assessment:

- Full history (consider current or recent SACT) + examination
- Assess urine output
- Urine, sputum + stool cultures
- Consider: throat swab, central line swab, wound swab and CXR

Signs of SEVERE sepsis - YES

- Altered mental state or
- Hypoxia (O^2 sats < 94%) **or**
- Shock (Systolic BP < 90 mmHg)
- Cold/clammy; Hyper/hypothermic; Tachycardic; Short of breath

Early signs of SIGNIFICANT sepsis - YES

- Temp > 38⁰C or < 36⁰C or
- HR > 90 and /or RR > 20 or
- Generally unwell. Infective symptoms; Shivering/rigors; Diarrhoea
- Raised lactate

Resuscitation Management:

- Resuscitation room or outreach team
- Optimise haemodynamics & O_2 delivery
- **ENSURE that 1st line intra-venous antibiotics have been administered**
- Transfer to HDU/ICU

Commence Neutropenic sepsis management:

- **ENSURE** that 1st line antibiotics have been administered, ***DO NOT DELAY*** for lab confirmation
- Supplemental O_2
- 1L 0.9% sodium chloride over 1-2 hours
- Differentiate between sepsis and neutropenic sepsis
- Supportive measures
- **Admit to appropriate area**

Identify: Potential sources of infection
Rx: Presenting complaint/co-morbidity
Tx: ECG, ABGs, Urinalysis, and Swabs
Do not perform a CXR unless clinically indicated

Further management guidance: proceed to page 20

TIME

On arrival

15 minutes

30 minutes

45 minutes

60 minutes

Ist line IV antibiotics in neutropenic sepsis as per NICE guideline:

- **Beta lactam monotherapy with piperacillin with tazobactam as initial empiric antibiotic therapy for patients with suspected neutropenic sepsis if there are no patient-specific or local microbiological contraindications.**
- **Patients with penicilin allergy should be discussed with the on call microbiologist**
- **Avoid aminoglycoside therapy in patients who have received platinum based chemotherapy in the last week**
- **Consider adding vancomycin /teicoplanin if CVAD is the suspected focus of infection**

https://www.nice.org.uk/guidance/cg151/chapter/1-Guidance#managing-suspected-neutropenic-sepsis-in-secondary-and-tertiary-care-2

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 12 continued. Suspected Neutropenic Sepsis

- Subsequent treatment should occur in an environment where appropriate skills and expertise are available.
- The patient should be closely monitored and the patient's risk of septic complications frequently reassessed using a validated risk scoring system (NICE 2012).
- If the patient continues to deteriorate despite initial treatment their condition should be discussed urgently with a senior clinician.

DAY ONE – Day of Admission		DAY TWO
	Monitoring	
National Early Warning Score Chart (**NEWS**) Every 15 minutes initially then regular monitoring according to patients condition.		NEWS Chart x 6 daily (every 4 hours) Daily FBC and U&E blood tests.
	Chemotherapy drugs	
Discontinue on admission; ensure safe disposal of unused chemotherapy		Do not recommence - requires oncology review.
	Antimicrobials	
Ist line antibiotics in neutropenic sepsis as per NICE guideline: Offer beta lactam monotherapy with piperacillin with tazobactam as initial empiric antibiotic therapy to patients with suspected neutropenic sepsis who need intravenous treatment unless there are patient-specific or local microbiological contraindications.		**Improving?** Assess if all antibiotics still required and route of administration. Discontinue empiric antibiotic therapy in patients whose neutropenic sepsis has responded to treatment, irrespective of neutrophil count. ***Unresponsive fever 48 hours?*** Do not switch initial empiric antibiotics in patients with unresponsive fever unless there is clinical deterioration or a microbiological indication. Continue inpatient therapy in all patients who have unresponsive fever unless an alternative cause of fever is likely.
Additional antimicrobials: Therapeutic monitoring/dose adjustment - Liaise with Pharmacy &Microbiology.		
Do not offer an aminoglycoside, either as monotherapy or in dual therapy, for the initial empiric treatment of suspected neutropenic sepsis unless there are patient-specific or local microbiological indications.		Consider viral and fungal infections, liaise with microbiology.
	Cultures	
Blood culture from central lines and peripherally, sputum, urine, swabs-throat & skin lesions. Liaise with microbiology prior to altering regimen. **Do not** remove CVADs as part of initial empiric management of suspected neutropenic sepsis. **NB.** CVADs may need to be removed in cases of severe sepsis, if unsure seek senior clinical support		Liaise with microbiology re interim results Re-culture patient before changing antimicrobials.
	Fluid and Electrolyte Balance	
Aggressive fluid replacement in dehydration. Hourly urine output measurement. Replace Na^+ and K^+ judiciously Early critical care management if deterioration, severe sepsis (any evidence of organ failure) or suspected invasive fungal infection.		Monitor fluid intake and output

Assess the patient's risk of septic complications according to NICE guidelines and MASCC score

Discharge only if:

- Low risk
- Physiologically stable
- When co-morbidity treated
- Neutropenic sepsis advice has been reinforced
- Discussed with a member of the acute oncology team prior to discharge

Guideline 13. **SKIN RASH (2 page guideline)** **Initial triage assessment within 15 minutes**

Skin rash can be a side effect of:

- **Systemic Anti Cancer Therapy**; Rash can be frequent and sometimes severe with:
  Targeted- agents: EGFR antagonists, BRAF and MEK inhibitors IV antibodies e.g. panitumumab/cetuximab.
  Immunotherapies 5-FU/capecitabine/sunitinib
- **Radiotherapy-** radiation toxicity
- **Graft versus host disease** in a patient who has undergone allogeneic stem cell transplant (**Contact haematology team**)
- **Illnesses or infection** e.g. shingles, chicken pox, impetigo, cellulitis, allergic reaction, meningitis.

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of allogeneic stem cell transplant. These patients may be myelosuppressed / neutropenic and are at risk of neutropenic sepsis and/or thrombocytopenia due to reduced marrow production or marrow infiltration and/or graft versus host disease: If present, this should be managed as per guideline 12 on P.19-20 - immediate antibiotics if sepsis suspected.

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&Es, LFTs, CRP, blood cultures if signs of systemic sepsis

Questions:

- Is there a cancer diagnosis/primary disease?
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop? Is skin rash a commonly associated and sometimes serious toxicity of their treatment, please see specific DRUG INFORMATION SHEET.
- Have they received **immunotherapy** proceed to guideline 26 page 35
- Have they received **oral targeted agents: EGFR antagonists, BRAF and MEK inhibitors**; see guideline 14 page 23
- Have they received **radiotherapy** recently: see guideline 15 on P.24
- Have they had a stem cell/ bone marrow transplant? If yes contact the haematology team.
- If the patient has received 5FU,Capcitabine: see guideline 16 on P.25
- Are they otherwise well? Does the patient have any signs of infection e.g. pain, swelling, pustules, fever, discharge?
- Has the patient recently started any other medication including antibiotics?
- Does the patient have a history of skin complaints?
- Where is the skin rash, what % BSA does it cover and what does it look like
- Does the rash itch? Itch only, consider liver/kidney problems/ dry skin/ allergy.
- Has the patient been in recent contact with infectious disease e.g. shingles/chicken pox?
- Does the patient have any other SACT toxicity related symptoms; if so please symptom specific guideline

Differential diagnosis includes:

- Side effect of medication
- Allergic reaction
- Infection
- Thrombocytopenia

Grade 1 (Green)

Rash covering <10% BSA, Macular/Papular eruption. Asymptomatic

- Provide appropriate skin care advice and emphasise the importance of skin care regimen (See P 22)
- Treat with emollient creams and antihistamines if required
- Ask patient to contact 24-hour advice line if symptoms worsen or persist

Grade 2 (Amber)

If any of the following are present:

- Pruritus, burning tightness
- Rash covering 10 -30% BSA
- Bleeding with trauma
- Affecting ADL or sleep

- Check all blood results and act on abnormalities
- Discuss with Haematology /Acute Oncology Team prior to discharge
- Treat symptomatically with emollient creams, antihistamines and consider topical or oral steroids. (See P.22)
- **IMMUNOTHERAPY see guideline 26 on P.35**
- Telephone/review patient within 24 hours ask patient to contact the 24-hour advice line if symptoms worsen/persist.

Grade 3/4 (Red)

If any of the following are present:

- Pruritic symptoms >30% skin surface
- Generalised
- Exfoliative
- Ulcerative
- Bullous dermatitis
- Spontaneous bleeding or signs of associated infection.

- Check all blood results and act on abnormalities
- For unusual, severe or persistent rash, particularly if the patient is unwell –urgent referral to dermatology
- Urgent admission if symptoms suggestive of Steven Johnson Syndrome or Toxic Epidermal Necrolysis
- Analgesia, fluid balance monitoring and skin care support and advice (see P.22)
- Consider admission for support and assessment.
- Determine cause and treat appropriately, this may include I.V. /oral or topical steroids.
- **IMMUNOTHERAPY see guideline 26 on P.35**
- **Oral targeted agents see guideline 15 on P.24**

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

UKONS Guideline 13. Continued. **SKIN RASH**

Initial management:
Assessment of fluid balance status, establish IV access if any signs of dehydration or sepsis
Intravenous fluids according to fluid balance status and renal function
Treat any infected lesions as appropriate and adjust antibiotics according to clinical condition, myelosuppression, swab results and local antibiotic guidelines
Delineate and record area affected area - photograph
Check platelet count – rash may be secondary to thrombocytopenia
If ulcers: Topical acyclovir for lips/oral acyclovir for herpes infection in mouth.

On-going management:
Reassess daily (close monitoring of routine observations as at risk of infection)
Observe for development of sepsis, neutropenia, or other chemotherapy toxicities
Fluid balance or daily weights
Daily full blood count
Dermatology review if concerns/uncertainty of diagnosis

Ensure general care measures:
Good fluid intake
Keep area clean and dry
Avoid hot baths/tight clothes
Mild soaps/cleansers/detergents

Consider Prescribing:
Topical creams/lotions (alcohol free, hypoallergenic e.g. E45) – apply regularly to all affected areas
Anti-histamines if rash causes itchiness
Analgesia if painful (caution with paracetamol/aspirin if risk of neutropenic sepsis)
Oral or topical steroids may be required.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 14. **Skin Toxicities -Targeted therapy-related** (Papulopustular rash)

Newer targeted anticancer therapies, particularly EGFR antagonists, BRAF, MEK and MTOR inhibitors, are frequently associated with skin toxicities, which are often seen in particular patterns and at different stages of treatment.

- **Papulopustular ("acneiform") rash:** predominately affects the scalp, face and upper trunk. Pruritus, irritation and pain may also be present
- **Xerosis ("dry skin"):** usually develops gradually and may present with eczema and/or fissuring
- **Nail changes:** include paronychia, onycholysis, splinter haemorrhages, and nail fold pyogenic granulomas
- **Hand-foot skin reaction:** dysaesthesia and paraesthesia can progress to localised, tender lesions, which may be bullous and severe. More common in plantar, pressure sites, heels and distal digits. Evolves to hyperkeratosis
- **Hair abnormalities:** classically a reversible inflammatory, non-scarring frontal alopecia. Hair growth is slowed and textural changes can occur. Increased hair growth is also seen, particularly of the eyelashes and eyebrows. Hypertrichosis can also involve the face and chest.

Initial Assessment

Observations: Calculate NEWS score.

Investigations: FBC, U&E

NB: Isotretinoin is not indicated for the treatment of papulopustular rash

Grade 1 (Green)

- Papules and/or pustules covering <10% BSA ± pruritus or tenderness

- Topical acne treatment (e.g 1% Clindarmycin lotion or gel)

Grade 2 (Amber)

- Papules and/or pustules covering 10-30% BSA ± pruritus or tenderness
- Limiting instrumental ADL
- Associated with psychosocial impact

- Topical emollients e.g. aveeno, epaderm, hydromol.
- Oral tetracyclines (e.g. lymecycline, doxycycline)
- Antihistamines for itch if required (hydroxyzine)

Grade 3 (Red)

- Papules and/or pustules covering >30% BSA ± pruritus or tenderness
- Limiting self-care ADL
- Associated with local superinfection

Grade 4 (Red)

- Papules and/or pustules covering any BSA ± pruritus or tenderness *and* are associated with extensive superinfection
- Life-threatening

- Consider delaying treatment
- As for grades 1 and 2
- If local superinfication - Oral antibiotics are indicated
- If extensive superinfection - IV antibiotics are indicated

General management and advice (and management of other skin toxicity patterns)

•*For hand-foot skin reaction, see guideline 16 on palmar-plantar erythrodysethesia (PPE)*
•Patients should be advised on general skin care at the commencement of treatment
•The use of soap substitutes, light emollients, sun cream and alcohol-free lotions should be advised
•Emollient creams are preferred over ointments as they can increase acneiform eruptions, e.g. aveeno, epaderm, hydromol.
•Topical or oral steroids may be required
•Avoid tight footwear and damage to the nail and surrounding skin if nail changes are observed
•Trichomegaly of the eyelashes can cause discomfort and trichiasis, which should prompt referral to an Ophthalmologist

Xerosis

- Eczema
  - Face & Neck: 1% hydrocortisone cream
  - Body: 0.05% clobetasone butyrate cream
  - Treat secondary bacterial superinfection as guided by microbiology swabs
- Fissures
  - Greasy emollients (e.g. Hydromol ointment, 50% propylene glycol under clingfilm or plastic glove occlusion)
  - Fludroxycortide impregnated tape *or* Zinc oxide paste with salicylic acid

Nail changes

- Inflammation of nail folds
  - Milton sterilising solution for 20 minutes daily
  - Topical steroid/antifungal (e.g. 1% hydrocortisone/miconazole cream)
- Purulent paronychia
  - Oral antibiotics
- Nail fold pyogenic granuloma
  - Curettage and cautery

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 15. Skin Rash - Radiotherapy reactions

- A skin reaction is a common side effect following radiotherapy treatment to the breast, head and neck, perineum, and skin, but may occur for any treated area.
- Commonly there is mild erythema and pruritus similar to mild sunburn, but the skin may get sore and break down.
- Patients are told to expect this after 10-14 days and can last for 4-6 weeks after completion of treatment.
- This is usually simple to manage but for patients with treatment of the head and neck or perineum, it can be severe, very painful, and impair function.
- Development of skin reactions depends on dose, fractionation, position and size of area treated, concurrent chemotherapy, and patient specific factors such as nutritional status

NB. If the patient is receiving or has recently received SACT treatment please see skin rash guideline 13 on P. 21-22

Grade 1 (Green)
Faint or dull erythema (RTOG1)

Head and Neck – E45
Skin-E45
Pelvis-E45
Breast- E45
Other-E45

Ask patient to contact the 24-hour advice line if symptoms worsen

Grade 2 (Amber)
Tender or bright erythema without moist desquamation (RTOG 2a)

Head and Neck – E45
Skin- Mepilex lite and E45 on surrounding areas
Pelvis-E45
Breast- E45
Other-E45
Analgesia may be required

- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist

Grade 3 (Amber)
Patchy moist desquamation, moist oedema (RTOG 2b)

- Appropriate conformable dressing as below:

Head and Neck – Mepilex Lite/Border (No Nu-Gel)
Skin- Mepilex Lite/Border
Pelvis- Nu-Gel, Sitz Bath and Fan Therapy
Breast- Mepilex Lite
Other-Mepilex Lite

- Swab area if signs of infection and prescribe antibiotics as required
- Analgesia for pain – may reqire opiates
- Telephone/review patient within 24 hours and arrange regular review with the radiotherapy team to assess progress.
- Ask patient to contact the 24-hour advice line if symptoms worsen

Grade 4 (Amber)
Confluent moist desquamation. (RTOG 3)

- Appropriate conformable dressing as below:

Head and Neck – Mepilex Lite/Border (No Nu-Gel)
Skin- Mepilex Lite/Border, Allevyn Gentle, Atrauman.
Pelvis- Nu-Gel, Sitz Bath, Fan Therapy and Instllagel (around urethra).
Breast- Aquacel, Mepilex Lite/Border
Other-Mepilex Lite/Border

- Swab area if signs of infection and prescribe antibiotics as required
- Analgesia for pain – may require opiates
- Telephone/review patient within 24 hours and arrange regular review with the radiotherapy team to assess progress.
- Ask patient to contact the 24-hour advice line if symptoms worsen

The advice above is for a guide only and each patient should be assessed individually. If unsure about products to use please seek further advice.

For further information please see - https://www.sor.org/learning/document-library/skin-care-advice-patients-undergoing-radical-external-beam-megavoltage-radiotherapy-0

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 16. **Skin toxicity - PALMAR - PLANTAR ERYTHRODYSESTHESIA** (Hand foot syndrome)

A distinctive localised cutaneous reaction to certain antineoplastic agents. Symptoms include: Tingling or burning, redness, flaking/dryness, swelling, small blisters, sores on palms and/or sole.

Identify: **Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic and at risk of sepsis. If present, this should be managed according to guidelines**

Observations: Calculate NEWS score.

Investigations: FBC, U&Es

Questions:

- What SACT regimen is the patient on? When was the last dose?
- Is this a continuous intravenous administration? E.g. 5-fluorouracil (5FU)
- Is the patient still taking oral SACT? E.g. capecitabine, sunitinib.
- Is the patient otherwise well? Any other symptoms e.g. diarrhoea/stomatitis (if yes refer to specific management guidelines) and contact the Acute Oncology Team.
- Have they experienced this side effect before on previous treatment cycles?
- Any signs of infection in the affected areas? – Discuss treatment options with the acute oncology team.

Grade 1 (Green)
Mild numbness, tingling, swelling of hands and/or feet, with or without pain or redness.

- Reassure the patient that this is recognised treatment related complication and generally nothing to worry about.
- Emphasise the importance of skin care regimen.
- Ask patient to contact 24-hour advice line if symptoms worsen.

Grade 2 (Amber)
Painful redness and or swelling of hands and/or feet.

- **Stop** the SACT until discussed with acute oncology or prescribing team.
- Reassure the patient that this is recognised treatment related complication and generally nothing to worry about.
- Emphasise the importance of skin care regimen.
- Consider prescription of high urea based cream.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

Grade 3 (Amber)
Moist desquamation, ulceration and severe pain in hands and or feet.

- **Stop** the SACT until discussed with the Acute Oncology Team. **If receiving Capecitabine or 5FU consider DPD deficiency**
- Review current analgesia (with caution as may not then develop a temperature in response to infection)
- Emphasise the importance of continuing skin care regimen.
- Consider prescription of high urea based cream.
- Consider specialist dermatology referral.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen.

Consider admission for further management if any signs of infection or other treatment related toxicities

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline17. VOMITING Initial triage assessment within 15 minutes

The forceful expulsion of the contents of the stomach through the mouth, and sometimes the nose.

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed / neutropenic fever and at risk of sepsis. If present, this should be managed according to guidelines

Observations: Calculate NEWS score.

Investigations: Urgent FBC, U&Es, CRP, LFTs, Magnesium, Ca^{2}+, Glucose, Blood cultures and CRP, Cortisol, (consider the need for pathology investigations in grade 1 presentations on an individual basis and in light of other presenting symptoms or risk factors)

Questions:

- Is there a cancer diagnosis/primary disease?
- What is the extent of the disease? – E.g. known metastases to brain, bone, liver etc.
- Is the patient taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- How often are they being sick? And are they also feeling nauseous?
- Assess bowel movements, any symptoms that suggest constipation? Any diarrhoea? Bowel obstruction?
- What food and fluids have been taking over last few days?
- Is there any evidence of reflux/gastritis?
- Are there any signs of dehydration e.g. decreased urine output, fever, thirst, dry mucous membranes etc.
- Are there any signs of infection?
- Are they taking any medication e.g. steroids, and has there been any recent change?
- Are they currently receiving radiotherapy? (Especially to brain, liver, GI Tract)
- Does the patient have any abdominal pain? Is this a new symptom?
- How is the patient fed? Do they have a feeding tube? Is this in the correct position?

Differential diagnosis includes:

- Medication related e.g. SACT
- Gastric stasis/ outlet obstruction
- Bowel obstruction
- Hypercalcaemia
- CNS disease
- Endocrinopathy
- Gastro intestinal infection
- Disease related
- Hyper-or-hypoglycaemia

MASSC guidelines here - http://www.mascc.org/antiemetic-guidelines

Grade 1 (Green)
1-2 episodes in 24 hours

- Review prescribed antiemetic medication make sure dose / route and frequency are appropriate and assess patient compliance and understanding
- Fully investigate cause:

Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.

Medication related e.g.SACT, opiates etc.

- When cause is clearly identified, change antiemetic in line with local policy directions
- Advise self help measures: https://www.macmillan.org.uk/information-and-support/coping/side-effects-and-symptoms/other-side-effects/nausea-and-vomiting.html#290074
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.

Grade 2 (Amber)
3-5 episodes in 24 hours

Initial advice as for grade 1

- Consider clinical review
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist.
- If symptoms worsen or are associated with other toxicities consider escalation to RED.

Grade 3 (Red)
6-10 episodes in 24 hours

Grade 4 (Red)
>10 episodes in 24 hours

- Admit for further assessment and management.
- IV fluids and electrolyte replacement as appropriate
- Fully investigate cause:
  - Disease related e.g. brain or liver metastases, electrolyte imbalance, and obstruction.
  - Medication related e.g.SACT, opiates etc. If receiving Capecitabine or 5FU consider DPD deficiency
- Consider placement of naso- gastric tube and nil by mouth order in suspicion of bowel obstruction
  Prescribe antiemetic as appropriate to cause in line with local policy
- Consider alternative route of administration of antiemetic's e.g. syringe driver
- Contact Acute Oncology/Haematology Team who may consider substitution, discontinuation of oral chemotherapy if appropriate.

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 18. Endocrinopathies Adrenal Crisis Immune-Related Adverse Event (irAE)

Immune checkpoint inhibitors **(ICPi)** have been causatively associated with a number of endocrinopathies, including hypophysitis, hypopituitarism and adrenal insufficiency. Patients may present with nonspecific symptoms, which may resemble other causes such as brain metastasis or underlying disease.

Endocrine function panel:
TSH, Free T4, free T3, ACTH, LH, FSH & cortisol prolactin, blood glucose +/- testosterone/oestrogen.
(9am cortisol is preferable but random cortisol measurement should be performed if the patient is unwell)
NB Values will be lab assay specific.

Mild – Asymptomatic (Grade 1)
Identified on routine blood test.
Biochemical alteration in cortisol with serum level < 450 mmol/L

Hypoadrenalism is likely if cortisol is <100mmol/L

Cortisol 100 - 450nmol/L
Investigations
Repeat cortisol at 9am within 48 hours
Endocrine function panel if outstanding
Actions
Monitor regularly (before each cycle as a minimum) and act as per algorithm if serum levels fall
Continue immune checkpoint inhibitors **(ICPi)**

Cortisol <100nmol/L
Investigations
Endocrine function panel if outstanding
Treatment
Commence hydrocortisone 10mg- breakfast
5mg –lunch, 5mg - dinner
Actions
Refer to endocrinology for advice/ further investigation
Give emergency advice/card about hydrocortisone
Continue **ICPi**

Moderate – Symptomatic (Grade 2)
Suspect endocrinology based on symptoms: Tiredness/fatigue, headache, weight loss, susceptibility to infection.

Investigations:
- Endocrine function panel if outstanding
- 9am cortisol and ACTH
- MRI brain with pituitary cuts

Cortisol (9am) >450 mmol/L
Adrenal insufficiency **unlikely**
Actions
Consider other causes of symptoms
Continue **ICPi**

Cortisol (9am) 100-450 mmol/L
Adrenal insufficiency **possible**
Actions
Endocrinology referral
Standard endocrine panel plus IGF-1
Continue **ICPi**

Cortisol (9am) <100nmol/L
Adrenal insufficiency **likely**
Treatment
Commence hydrocortisone
10mg- breakfast
5mg –lunch, 5mg - dinner
Actions
Endocrinology referral
Standard endocrine panel plus IGF-1
Give emergency advice/card about hydrocortisone
Continue **ICPi**

Severe or Life-threatening (Grade 3 + 4)
Suspect adrenal crisis:
Hypovolemic shock
Hypotension –SBP <90mm Hg
Postural hypotension ->20mm Hg drop
Dizziness/Collapse
Nausea/Vomiting
Abdominal pain/tenderness/guarding
Fever
Confusion/delirium/coma
Hyponatraemia/hyperkalaemia
hypoglycaemia
Pre-renal failure
Severely unwell patient: severe dehydration, abdominal pain, or shock

Investigations:
- Send endocrine function panel bloods immediately
- **Admit patient**
- Immediate management with an ABCDE approach
- **Immediate bolus injection of 100 mg hydrocortisone i.v. or i.m. followed by continuous intravenous infusion of 200 mg hydrocortisone per 24 h** (alternatively50 mg hydrocortisone per i.v. or i.m. Injection every 6 h)
- **Rehydration** with rapid intravenous infusion of 1000 mL of isotonic saline infusion within the first hour, followed by further intravenous rehydration as required (usually 4–6 L in 24 h; monitor for fluid overload in case of renal impairment and in elderly patients)
- **Urgent Endocrinology referral** for urgent review of the patient, advice on further tapering of hydrocortisone, investigation of the underlying cause of disease including diagnosis of primary vs secondary adrenal insufficiency
- Rule out superadded infections
- **Withhold** the next cycle of **ICPi**

CAUTION:
- If a delay in endocrinology review is anticipated then commence hydrocortisone - 10mg- breakfast, 5mg –lunch, 5mg – dinner. This will ensure patient safety until endocrinology review.
- If the patient is currently on steroids (prednisolone/dexamethasone) then serum cortisol will likely be suppressed – please discuss with the endocrinology team before commencing replacement.
- If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced for 24 - 48 hours prior to commencing thyroid replacement (for which the grade 1 hypothyroidism guidelines should be instituted – guideline 20 P.29)

Society for Endocrinology **[SfE]** guidelines for adrenal crisis:
www.endocrineconnections.com/content/5/5/G1

ESMO Guidelines - http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Clinical presentation
Typically, hypophysitis presents with headache, fatigue and visual loss. There are a range of non-specific symptoms including nausea, diarrhoea, malaise and anorexia, which may represent pituitary dysfunction and a low threshold for clinical suspicion is required. However, these typical symptoms are common in patients with complications of cancer undergoing SACT and other differentials, such as CNS metastases need to be considered.

Endocrine function panel:
TSH, Free T4, free T3, ACTH, LH, FSH & cortisol prolactin, blood glucose +/- testosterone/oestrogen.
(9am cortisol is preferable but random cortisol measurement should be performed if the patient is unwell)
NB Values will be lab assay specific.

- Vague symptoms:
  - Mild fatigue
  - Anorexia
- No headache
  or
- Asymptomatic

Investigations
- Complete endocrine function panel
- FBC, U&E, LFT
- MRI pituitary protocol to confirm diagnosis- exclude cerebral metastases
- Consider formal visual field assessment
- NEWS monitoring

Actions
- **Refer to endocrinology**
- Replace cortisol and/or thyroxine according to endocrinology guidance. Refer to IrAE management guidance on treatment of hypoadrenalism and thyroid dysfunction for replacement doses and further management – Guideline 18, P.27
- Withhold ICPi until symptoms controlled and consider restarting once patient stable

Moderate symptoms:
- Headache but no visual disturbance

or
- Fatigue/mood alteration but haemodynamically stable, no electrolyte disturbance.

Investigations:
- Complete endocrine function panel
- FBC, U&E, LFT
- MRI pituitary protocol to confirm diagnosis- exclude cerebral metastases
- Consider formal visual field assessment
- NEWS monitoring

Treatment:
- Consider oral prednisolone 0.5-1 mg/kg /day to reduce pituitary oedema, if headaches or neurological problems are present
- Start steroid therapy after sending endocrine function panel

Actions:
- **Refer to endocrinology**
- Replace cortisol and/or thyroxine according to endocrinology guidance. Refer to IrAE management guidance on treatment of hypoadrenalism and thyroid dysfunction for replacement doses and further management – Guideline 18, P.27
- Withhold ICPi until symptoms controlled and consider restarting once patient stable

Severe mass effect symptoms such as:
- Severe headache
- Any visual disturbance

or
Severe hypoadrenalism i.e.
- Hypotension
- Severe electrolyte disturbance

Investigations:
- Complete endocrine function panel
- FBC, U&E, LFT
- MRI pituitary protocol to confirm diagnosis- exclude cerebral metastases
- Consider formal visual field assessment
- NEWS monitoring

Treatment:
- Consider i.v. Methylprednisolone 1 mg/kg /day to reduce pituitary oedema, if headaches or neurological problems are present
- Start steroid therapy after sending endocrine function panel
- Analgesia for headache

Actions:
- **Refer to endocrinology**
- **Admit to hospital –** Replace cortisol and/or thyroxine according to endocrinology guidance. Refer to IrAE management guidance on treatment of hypoadrenalism and thyroid dysfunction for replacement doses and further management – Guideline 18, P.27
- **Withhold ICPi** until symptoms are controlled and consider restarting once patient is stable.

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance

PERSIST > 48 hours
WORSEN or RELAPSE

CAUTION: If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced for 24 - 48 hours prior to commencing thyroid replacement (for which hypothyroidism guidelines should be instituted – guideline 20 P.29)

Society for Endocrinology **[SfE]** guidelines for adrenal crisis: www.endocrineconnections.com/content/5/5/G1

ESMO Guidelines - http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 20. Endocrinopathies - Thyroid Dysfunction Immune-Related Adverse Event (irAE)

Immune checkpoint inhibitors (**ICPi**) have been causatively associated with a number of endocrinopathies, including hypo/hyperthyroidism. Observational studies have shown that there is a typical pattern of thyroid specific biochemical disturbance presenting with asymptomatic hyperthyroidism, before return to normal levels for a brief period. This is nearly always followed by the development of, in some cases profound, hypothyroidism that is frequently persistent and requires long-term thyroid replacement. Smaller subsets of patients develop isolated hypothyroidism over a period of weeks. Both groups appear to require long-term replacement in a majority of cases.
Thyroiditis and autoimmune Grave's disease hyperthyroidism can occur as well as primary hypothyroidism.

Endocrine function panel:
TSH, Free T4, free T3, ACTH, LH, FSH & cortisol prolactin, blood glucose +/- testosterone/oestrogen.
(9am cortisol is preferable but random cortisol measurement should be performed if the patient is unwell)
NB Values will be lab assay specific.

Hypothyroidism
TSH of >10 mULN and Free T4 < lower limit of normal (LLN)
NB Values will be lab assay specific.

Symptoms: Fatigue – Weakness - Sensitivity to cold Weight gain or difficulty losing weight - Coarse, dry hair and dry skin - Hair loss - Muscle cramps and aches – Constipation – Depression – Irritability -Memory loss - Abnormal menstrual cycles -Decreased libido - Slowed speech (severe cases) - Jaundice (severe cases) - Increase in tongue size (severe cases)

Investigations:
- Endocrine function panel if outstanding

Treatment:
- Commence Levothyroxine at 75 mcg or 25 mcg for high risk patients
- Consider starting Levothyroxine at 25 micrograms in profoundly hypothyroid patients to avoid palpitations
- **Caution** with high risk patients - history of/or existing cardiac conditions e.g. Atrial fibrillation and elderly patients

Actions:
- Recheck TFTs and cortisol with next cycle of treatment – note TSH will not fall for 4-6 weeks after starting levothyroxine.
- Discuss with endocrinologist to identify best pathway for long-term management and monitoring (primary/secondary care)
- **Refer to endocrinologist if unable to stabilise thyroid function**
- Continue **ICPi**

CAUTION: If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced for 24 - 48 hours prior to commencing thyroid replacement (for which hypothyroidism guidelines should be instituted – guideline 20 P.29)

Society for Endocrinology **[SfE]** guidelines for adrenal crisis: www.endocrineconnections.com/content/5/5/G1

ESMO Guidelines - http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Hyperthyroidism
TSH <0.40 mULN and Free T4 > upper limit of normal (ULN)
NB Values will be lab assay specific.
(If TSH low and T4 normal or low need to exclude pituitary dysfunction)
Check TSH receptor antibodies
Symptoms: fatigue or muscle weakness - hand tremors – mood swings - nervousness or anxiety - rapid heartbeat - heart palpitations or irregular heartbeat- skin dryness- trouble sleeping - weight loss -increased frequency of bowel movements – menstrual disturbance

Investigations:
- Endocrine function panel if outstanding

1. Asymptomatic

The majority of cases become hypothyroid within a matter of weeks.

Actions:
- Recheck TFTs and cortisol within 1- 2 weeks and every 1-2 weeks thereafter.
- Once hypothyroid - manage as per hypothyroidism

2. Symptomatic

The majority of cases become hypothyroid within a matter of weeks.
If persistent manage in collaboration with an **endocrinologist**

Added Investigations:
- TSH Receptor Ab, anti-TPO Ab, nuclear medicine thyroid uptake scan
- **Treatment:**
- Consider B-blocker - Propranolol or Atenolol
- Painful thyroiditis – consider prednisolone 0.5mg/kg and taper
- Consider Carbimazole if TSH Receptor Ab positive – seek endocrinology advice
- **Actions:**
- Recheck TFTs and cortisol within 1- 2 weeks and every 1-2 weeks thereafter.
- Once hypothyroid - manage as per hypothyroidism
- If **unwell withhold ICPi** and consider restarting when symptoms controlled

Always make sure that the Acute Oncology Team are informed of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 21. Gastro Intestinal Immune-Related Adverse Event (irAE)

Gastrointestinal (GI) irAEs are among the most common, if they are left unrecognised or untreated, they can become life threatening. These toxicities can be managed effectively in almost all patients by using established guidelines that stress vigilance and the use of corticosteroids and other immunosuppressive agents when necessary.

As with all **irAEs** this can be a delayed effect of treatment and can occur up to 12 months after completion of treatment

Mild (Grade 1)

< 4 stools/day over baseline *or* mild increase in ostomy output
NO history of abdominal pain, mucous/blood in stools

Management Plan:

Investigations:

- ☐ Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- ☐ Stool microscopy and culture
- ☐ Clostridium difficile toxin
- ☐ Faecal calprotectin (if symptoms persist)

Treatment:

- Loperamide (use with caution as may mask symptoms of worsening colitis)
- Encourage fluids
- Avoid high fibre and lactose

Actions:

- Telephone assessment within 3 days
- Continue Immune checkpoint inhibitors unless on combination anti-PD1/CTLA4 then consider **withholding** treatment

Symptoms: PERSIST (≥5 days) or WORSEN or are associated with deranged U & E's

CAUTION – discontinue loperamide and/or codeine in patients with moderate to severe symptoms as these drugs increase the risk of colonic dilatation and perforation.

Moderate (Grade 2)

If **any** of the following symptoms are present:

- 4-6 stools/day over baseline *or* moderate increase in ostomy output
- Moderate abdominal pain/cramps/discomfort
- Mucous in stool regardless of number of stools
- Nocturnal stools
- Persistent grade 1 symptoms

Management Plan:

Investigations:

- ☐ Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- ☐ Stool microscopy and culture
- ☐ Clostridium difficile toxin
- ☐ Faecal calprotectin (if symptoms persist)
- ☐ Polymerase Chain Reaction **(PCR) screen**
- ☐ Abdominal X-Ray and consider CT abdomen/pelvis.

Treatment:

- Prednisolone 0.5-1 mg/kg/day + PPI cover
- STOP Loperamide and codeine
- Fluid balance and replacement as appropriate (inc. diarolyte sachets)

Actions:

- Withhold next dose of **ICPi**
- Daily telephone monitoring
- Gastroenterology advice/review (consider endoscopy).

Assess response to treatment within 72 hours

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance

PERSIST
WORSEN
RELAPSE

Severe or Life-Threatening (Grade 3 + 4)

If **any** of the following symptoms are present:

- ≥6 stools/day over baseline *or* significant increase in ostomy output
- Severe abdominal pain
- Fever
- Dehydration
- Blood in stool
- Incontinence
- Limiting ADLs
- Episodes within 1 hour of eating

Admit patient

Investigations:

- ☐ Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- ☐ Stool microscopy and culture
- ☐ Clostridium difficile toxin
- ☐ Faecal calprotectin (if symptoms persist)
- Daily bloods (FBC, U&E, LFTs & CRP)
- CT Abdomen/pelvis
- Flexible sigmoidoscopy with biopsies (inc. CMV staining)
- Screen for Infliximab administration suitability on admission to avoid delay if treatment is required (to include-TB Eli spot test, hepatitis screen, HIV, chest X-Ray (if chest CT not already performed)

Refer and review by gastroenterologist

Treatment:

- IV hydration and fluid balance
- IV Methylprednisolone 1-2 mg/kg/day + PPI cover
- Antibiotics are not required as standard
- STOP loperamide and codeine

Use analgesia with CAUTION

Actions:

- Daily stool chart
- Consider nothing by mouth or clear fluids
- Dietician review
- Withhold and consider discontinuation of **ICPi**

PERSIST ≥ 3 days IV corticosteroids

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Review patient daily, if no improvement within 72 hours, seek further urgent gastroenterology advice/opinion for management with infliximab.

http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Guideline 22. Hepatotoxicities Immune-Related Adverse Event (irAE)

Hepatic transaminases (ALT/AST) and bilirubin must be evaluated before each dose of immunotherapy, as early laboratory changes may indicate emerging immune-related hepatitis. Elevations in LFTs may develop in the absence of clinical symptoms. This guidance should be used in context of baseline LFTs and presence of known liver metastases.

Mandatory investigations and actions at initial assessment:

- LFTs
- Amylase
- AST/ALT
- gGT
- CK
- Clotting (INR)
- Lactate/acidosis
- Ferritin
- EBV/CMV
- HSV & parvovirus
- Hepatitis PCR screen
- Auto immune screen
- Hepatitis ABCE screen
- Split bilirubin if bilirubin is markedly elevated
- FBC – document cytopenia especially lymphopenia and monoctyopenia
- Ultra Sound Scan in the first 12- 24 hours to assess spleen size and include doppler to assess flow in hepatic veins and arteries

Observations: Monitor and document Glasgow Coma Scale and NEWS

Mild (Grade 1)
AST or ALT > ULN = 3 x ULN

- Continue treatment
- Repeat LFT's in 1 week - if rising escalate

Moderate (Grade 2)
AST or ALT >3 to ≤5 x ULN

Investigations:
- **Re-check LFTs and INR every 3 days**
- Consider imaging for metastases/clot
- Consider checking paracetamol levels.
- **Treatment:**
- Commence prednisolone 1mg/kg/day (max 60mg OD)

Actions:
- Withhold ICI treatment until the adverse reaction resolves to Grade 0-1 or returns to baseline.
- **Medications Review: STOP regular paracetamol, NSAIDs.**
- Concomitant medications can exacerbate liver toxicity in this scenario. Therefore **discontinuation of ALL** non-essential medication is advisable on admission.

Severe or Life-Threatening (Grade 3/4)
AST or ALT >5 x ULN (Grade 4 >20 x ULN)

Admit to hospital
Early/Urgent referral to hepatologist required

Investigations:
- **Daily LFTs / INR /Albumin**
- Consider checking paracetamol levels.

Treatment:
- **Steroids**

Grade 3 –
- If ALT/AST <400 and normal bilirubin/INR/albumin - **oral** prednisolone 1mg/kg/day.
- If ALT/AST >400 or raised bilirubin/INR/albumin - **IV** methylprednisolone 2mg/kg/day.

Grade 4 - IV methylprednisolone 2mg/kg/day
- **Consider IV N-acetylcysteine (NAC 150mg/Kg as loading dose and 150mg/Kg over 24 hours for patients in grade 3 or 4 toxicity**
- Consider antibiotic and antifungal prophylaxis for patients receiving methylprednisolone.

Actions:
- **Medications Review: STOP regular paracetamol, NSAIDs.**
- Concomitant medications can exacerbate liver toxicity in this scenario. Therefore **discontinuation of ALL** non essential medication is advisable on admission
- Discuss requirements for CT scan after USS with hepatologist
- Discuss requirements for liver biopsy with hepatologist
- If Grade 3 withhold next cycle of treatment
- If Grade 4 discontinue treatment permanently

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance – see guideline 27, P.36

Biochemical Abnormality PERSISTS (≥3 days), WORSEN or RELAPSE

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance – see guideline 27, P.36

Review patient daily, if no improvement within 72 hours, seek urgent hepatologist advice /review regarding on-going management –patients may require further treatment with immunosuppressive drugs, such as MMF or Tacrolimus.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Guideline 23. Neurological Immune-Related Adverse Event (irAE)

Neurologic irAEs can manifest as central abnormalities (e.g., aseptic meningitis, encephalitis) or peripheral sensory/motor neuropathies (e.g., Guillain-Barre Syndrome). Early recognition and treatment of neurologic irAEs is critical to its management. As neurologic symptoms can be common in subjects with cancer, it is important that an evaluation/work-up distinguish between non-drug-related causes (e.g. progression of disease, concomitant medications, infection) and a possible drug-related AE as the management can be quite different.

Mild (Grade 1)
- Asymptomatic;
- Loss of deep tendon reflexes or paraesthesia (including tingling);
- Not interfering with function or ADLs not concerning to patient

Moderate (Grade 2)
- Sensory alteration or paraesthesia (including tingling)
- Some interference with function
- Cranial nerve problem
- Symptoms concerning to patient

Severe or Life-Threatening (Grade 3-4)
- Severe or disabling symptoms;
- Limiting self-care ADLs
- Life-threatening (e.g. respiratory problems)

Is there any cranial nerve involvement?

Yes

No

Management Plan

Management:
- Regular close monitoring for progression
- Consider withholding **ICPi** for 1 week whilst monitoring

Investigations:
- Comprehensive neurological exam
- Review alcohol and medications history - opiates
- FBC, U&E, ALT, cortisol, TFT's, glucose, B12 and folate HIV, TSH
- Consider autoimmune and vasculitis screen
- Consider MRI/MRA brain /spine +/- CSF exam to exclude other causes e.g. CVA, brain metastases.

WORSEN

Resolved or Improved (Grade 1)
Continue with **iCPi**

Investigations:
- Neurological examination
- FBC, U&E, ALT, cortisol, TFT's, glucose, B12 and folate, HIV, TSH
- Consider autoimmune and vasculitis screen
- Consider MRI/MRA brain /spine +/- CSF exam to exclude other causes e.g. CVA, brain metastases.
- Alcohol history and medications - opiates
- Special investigations guided by clinical picture of specific disorders
- Consider nerve conduction studies or EMG for lower motor neuron and/or sensory changes
- Consider pulmonary function, sniff, and diaphragmatic function tests

Management:
- Delay **ICPi**
- Daily monitoring for progression
- Consider neurology referral and review
- Treat symptoms per local guidelines
- Consider IV methylprednisolone 0.5-1mg/kg/day methylprednisolone or oral prednisolone 0.5-1mg/kg/day (max. 60mg/day) + PPI
- Consider pregabalin or duloxetine for neuropathic pain
- Consider orthotic devices

PERSIST > 5 days
WORSEN or RELAPSE

Investigations:
- Daily neurological review
- Regular NEWS and GCS score
- FBC, U&E, ALT, cortisol, TFT's, glucose, B12 and folate, HIV, TSH
- Serum creatinine Kinase (CK)
- Alcohol history and medications
- Consider daily vital capacity test
- MRI /MRA brain or spine to exclude any other causes
- Nerve conduction studies
- Electromyography
- Lumbar puncture
- Muscle biopsy
- Pulmonary function tests

Management Plan

Neurology referral and urgent review

Permanently discontinue **ICPi**

Management:
- Hospital admission
- Commence IV hydration
- IV methylprednisolone 1-2mg/kg/day (or IV equivalent) + PPI
- Consider orthotic devices
- Treatment for specific disorders
- Ophthalmology review for ocular involvement

PERSIST > 5 days
WORSEN or RELAPSE

Management Plan

Under guidance of neurology team

Management escalation:
- Consider IVIG or other immunosuppressive therapies
- Treatment for specific disorders

Resolved or Improved (Grade 1)

Management Plan
- Discontinue Immune checkpoint inhibitors (**ICPi**) permanently
- **See steroid taper guidance guideline 27 P.36**

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible. Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Guideline 24. Pneumonitis Immune-Related Adverse Event (irAE)

Pulmonary irAEs have been observed following treatment they have occurred both after a single dose and after as many as 48 treatments. The frequency of pulmonary AEs may be greater with immunotherapy combination therapies than with monotherapy and more common in lung cancer than in melanoma. The majority of cases reported were Grade 1 or Grade 2 and presented with either asymptomatic radiographic changes (e.g. focal ground glass opacities, patchy infiltrates) or with symptoms of dyspnoea, cough, or fever. Subjects with reported Grade 3 or Grade 4 pulmonary AEs were noted to have more severe symptoms, more extensive radiographic findings, and hypoxia.

Mild (Grade 1)
Clinically asymptomatic *with* Radiographic changes only
(e.g. focal ground glass opacities, patchy infiltrates)

Clinical Assessment & O2 SATS
Investigations:
- Sputum sample for MC&S and PCP PCR
- Baseline bloods (FBC, U&Es, LFTs, CRP, calcium)
- Chest X-ray - baseline for further assessments
- High resolution CT Scan **(HR CT)**

Actions:
- Monitor symptoms every 2-3 days and re-image if worsening
- Consider delay of **ICPi**

WORSEN

Moderate (Grade 2)
Mild to moderate new onset of symptoms limiting instrumental ADL
(e.g. dyspnoea, cough, fever, chest pain)

Clinical Assessment & O2 SATS
Investigations:
- Sputum sample for MC&S
- Baseline bloods (FBC, U&Es, LFTs, calcium, CRP)
- High Resolution CT imaging (HR CT)
- Bronchoscopy +/- lavage

Treatment:
- If no evidence of infection commence Prednisolone 0.5 - 1mg/kg/day (max. 60mg/day prednisolone) + PPI
- Consider antibiotics **(ABX)** If evidence of infection

Actions:
- Hold **ICPi**
- Consider hospital admission
- Refer to a chest physician
- Monitor symptoms daily with clinical examination review if symptoms worsening (with repeat imaging)

Assess response to treatment within 48 hours

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance – see guideline 27, P.36

PERSIST
WORSEN or
RELAPSE

Severe/Life-Threatening (Grade 3+ 4)
Severe new onset of symptoms limiting self-care ADL; *or* Hypoxia (new or worsening); *or* Acute Respiratory Distress Syndrome (**ARDS**)

Admit patient
Refer to specialist chest physician

Clinical Assessment & O2 SATS
Investigations:
- Sputum sample for MC&S
- Baseline bloods (FBC, U&Es, LFTs, calcium, CRP)
- High Resolution CT imaging (HR CT)
- Bronchoscopy if condition allows
- +/- Pulmonary function test

To exclude atypical infections:
- Galactomannan and Beta-D-glucan
- Urine legionella and pneumococcal antigen
- Mycoplasma serology
- Pneumocystis Jiroveci Pneumonia (**PJP**) screening

Treatment:
- IV Methylprednisolone 2mg/kg/day + PPI
- Consider *increasing* to 4mg/kg/day *if* clinical improvement is unsatisfactory
- Consider empiric ABX and antifungal therapy

Actions:
- Discontinue **ICPi**
- Monitor symptoms daily with clinical examination, if symptoms worsening, repeat imaging is required
- Manage symptoms accordingly
- Consider the use of Infliximab if no improvement at 48 hrs. – discuss with chest physician

Please see Guideline 27 on P.36 for advice regarding management of patients receiving high dose or long-term steroids

Continue with daily review, if no improvement within 72 hours; seek chest physician advice/review for further management

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Guideline 25. Renal Toxicities Immune-Related Adverse Event (irAE)

Elevated creatinine and biopsy confirmed tubulointerstitial nephritis and allergic nephritis have been infrequently observed following treatment with immunotherapy agents. The frequency of renal AEs may be greater with combination therapies than with monotherapy. Most cases were Grade 2 or Grade 3 and based on creatinine elevation. Patients with a history of RCC or prior nephrectomy do not appear to be at higher risk. Events were managed with corticosteroids and in all cases renal function partially or fully improved.

Mild (Grade 1)
Creatinine < 1 – 1.5 x increase from baseline
= Stage 1 AKI

Investigations:
- Weekly creatinine monitoring

Actions:
- Ensure well hydrated
- Continue **ICPi**
- Review concomitant medication and stop nephrotoxic drugs

WORSEN

Moderate (Grade 2)
Creatinine > 1.5 - ≤ 3 x increase from baseline
= Stage 2 AKI

Clinical Assessment

Investigations:
- Vital signs
- FBC, U&E, ALT, cortisol, TFTs and glucose
- Urinalysis-
- *Protein positive*- urine sample protein creatinine ratio
- *Blood positive*- urine sample to microbiology for casts
- If blood and protein in urinalysis send for both -protein creatinine ration and casts

Treatment:
- If clear urinalysis-institute adequate hydration, withhold nephrotoxins and repeat blood in 24 – 48 hours
- If positive urinalysis commence 1mg/kg/day oral prednisolone + PPI
- **Actions:**
- Monitor creatinine every 48 hours
- Exclude other causes
- Review concomitant medication and stop nephrotoxic drugs
- **Prompt** Referral to renal team for further advice - consider renal biopsy/USS
- HOLD **ICPi** until adverse reaction resolves to Grade 1 or Grade 0 (or returns to baseline)

Severe or Life-Threatening (Grade 3 + 4)
Creatinine > 3 x ULN
= Stage 3 AKI

Admit patient
Urgent referral to renal team for renal biopsy/USS and urgent advice

Investigations:
- Vital signs
- FBC, U&E, ALT, cortisol, TFTs and glucose
- Urinalysis-

* *Protein positive*- urine sample protein creatinine ratio
* *Blood positive*- urine sample to microbiology for casts
* If blood and protein in urinalysis send for both -protein creatinine ration and casts
- Daily weight
- Exclude other causes
- Monitor creatinine daily
- Fluid balance

Treatment:
- IV methylprednisolone 1-2mg/kg/day + PPI
- IV hydration as indicated

Actions:
- Discontinue **ICPi**
- Review concomitant medication and stop nephrotoxic drugs

Detect AKI by using one of the following criteria:

A rise in serum creatinine of 26micromol or greater within 48 hours

A 50% or greater rise in serum creatinine known or presumed to have occurred within the past 48 hours

A fall in urine output to less than 0.5ml/Kg/hour for more than 6 hours in adults and 8 hours in young people

A 25% or greater fall in eGFR in young people in the last 7 days

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance – see guideline 27, P.36

Symptoms: PERSIST (≥ 5 days) or WORSEN or RELAPSE

Review patient daily, if no improvement within 72 hours, seek nephrologist advice for further management

Symptoms: Resolve or Improve to Mild
See steroid tapering guidance – see guideline 27, P.36

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

- https://pathways.nice.org.uk/pathways/acute-kidney-injury
- http://www.kdigo.org/clinical_practice_guidelines/pdf/KDIGO%20AKI%20Guideline.pdf

Guideline 26. Skin Toxicities Immune-Related Adverse Event

Dermatological irAEs common and although they are typically mild to moderate in severity, if left unrecognised or untreated, they can become life-threatening. These toxicities can be managed effectively in almost all patients by using established guidelines that stress vigilance and the use of corticosteroids and other immunosuppressive agents when necessary.

Grade 1
Skin rash, affecting <10% Body Surface Area (BSA) with or without symptoms
And
Grade 2 (Moderate)
Skin rash affecting 10% - 30% of BSA with or without symptoms

Clinical Assessment:
- Exclude other causes e.g. virus, medication
- **If substantial symptoms present – escalate to Grade 3**

Investigations:
- Vital signs
- FBC, U&E, ALT, cortisol, TFTs and glucose
- Photograph rash
- Measure lesions

Treatment:
- Anti-histamines – topical or oral
- Topical steroids
- Topical emollient

Actions:
- Regular monitoring- consider daily review
- Skin care advice
- Consider dermatology referral and skin biopsy
- Continue **ICPi** treatment as planned

WORSEN

Grade 3
Skin rash affecting>30% of BSA or grade 2 with substantial symptoms

Clinical Assessment:
- Exclude other causes e.g. virus
- If severe symptoms e.g.exfoliative, ulcerative, purpura – escalate to red

Investigations:
- Vital signs
- FBC, U&E, ALT, cortisol, TFTs and glucose
- Photograph rash
- Measure lesions

Treatment:
- **Mild to moderate** - Prednisolone 0.5 – 1mg/kg /day for 3 days then taper over 1-2 weeks+ PPI
- **Severe –** i.v. Methylprednisolone 0.5 -1mg/kg /day and convert to oral on response, taper over 2-4 weeks + PPI
- Anti-histamines
- Emollient with paraffin content

Actions:
- **Withhold ICPi** treatment
- Dermatology review - consider punch biopsy
- Monitor daily
- Consider admission to hospital if clinically indicated.

Symptoms: Resolve or Improve to grade1-2
See steroid tapering guidance – see guideline 27, P.36

PERSIST (≥5 days), WORSEN or RELAPSE

Grade 4
Skin sloughing >30% BSA with associated symptoms:
- Generalised
- Exfoliative
- Ulcerative
- Bullous dermatitis
- Purpura

Clinical Assessment:
- Exclude other causes e.g. virus
- Admit patient for monitoring and further management
- **URGENT dermatologist review**

Investigations:
- Vital signs – NEWS monitoring
- FBC, U&E, ALT, cortisol, TFTs and glucose
- Punch biopsy
- Fluid balance assessment and monitoring
- Photograph rash
- Measure lesions

Treatment:
- Commence IV hydration in cases of extensive bullous/desquamating rashes
- i.v. methylprednisolone 1-2 mg/kg/day + PPI
- Anti-histamines
- Analgesia
- Emollient
- Antibiotics are not indicated unless there is a concern of recurrent infections and/or recommended by treating clinician

Actions:
- Discontinue **ICPi** permanently

Symptoms: Resolve or Improve to grade1-2
See steroid tapering guidance – see guideline 27, P.36

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.esmo.org/Guidelines/Supportive-and-Palliative-Care/Management-of-Toxicities-from-Immunotherapy

Guideline 27. Management of patients receiving high dose or long-term steroids for irAE's

Many patients will receive moderate- to high-dose steroid therapy for their immune-related toxicity for several weeks. Length of tapering is usually dictated by the severity of the irAE. Regular monitoring during tapering is strongly advised, as there is an increased risk of irAE recurrence. PPI cover should be maintained during tapering process.

Steroid tapering should only be considered when symptoms are improving.

Suggested oral steroid tapering:

- Corticosteroid taper over at least 3-6 weeks
- Reduce prednisolone dose by 10mg every 3 -7 days (as toxicity allows) until dose is 10mg/day.
- Once steroid dose is 10mg/day, reduce by 5mg every 5 - 7 days then stop.
- Patients will need regular blood test and symptom monitoring during tapering
- Ambulatory monitoring may be possible with regular telephone review and local blood testing

Suggested intravenous steroid tapering:

- Corticosteroid taper over at least 6 weeks
- Continue IV methylprednisolone 2mg/kg/day for a total of 3-5 days then switch to oral e.g. prednisolone max. 60mg/day.
- Methylprednisolone 1mg/kg/day x 3 days, then switch to oral e.g. prednisolone max. 60mg/day.

Upon discharge:

- Reduce prednisolone dose by 5 to 10mg every 7 days (as toxicity allows) until dose is 10mg/day.
- Patients will need regular blood test and symptom monitoring during tapering
- Ambulatory monitoring may be possible with regular telephone review and local blood testing

CAUTION - during and after the tapering process as the adrenal axis may be suppressed and there is a risk of iatrogenic hypoadrenalism– if symptoms occur follow adrenal crisis guidance – guideline 18 on P.27.

Insomnia:

This is the most common steroid-related side effect. Sleep hygiene counseling is important. Patients may require short-term use of 1st line treatment for insomnia e.g.zopiclone.

Hyperglycaemia:

A baseline HbA1c should be requested at steroid initiation and random afternoon blood sugar monitoring (BM) should be undertaken whilst on treatment. If new hyperglycemia is detected, Endocrinology advice should be sought (many patients will require short term insulin in this setting). Pre-existing diabetes may require escalation in oral hypoglycemic agents or insulin.

Osteoporosis:

Vitamin D and calcium levels should be taken at baseline and if low, replaced as appropriate. In patients on steroids for >3 months, or with pre-existing osteoporosis, a bisphosphonate should be considered e.g. weekly alendronic acid

Infection:

In patients receiving the equivalent of prednisolone 25mg for ≥ 6 weeks we suggest PJC prophylaxis with co-trimoxazole (80/400mg Mon/Wed/Fri).

Prophylactic antifungals i.e. Fluconazole and monitoring of patients oropharynx.

If patients are on other immuno-modulatory agents e.g. Mycophenylate mofetil, consideration may be given to CMV prophylaxis with valgancyclovir, especially if CMV IgG negative and lymphopenic.

Guideline 28. ABDOMINAL ASCITES (Management Pathway)

Ascites is the accumulation of protein rich fluid in the peritoneal cavity and can be classed as an exudate or transudate. Ascites typically develops in the setting of recurrent and/or advanced cancer, the commonest sites being ovarian, breast and colo-rectal.

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of stem cell transplant. These patients may be myelosuppressed /neutropenic and at risk sepsis. If present, this should be managed according to guidelines.

Observations: Calculate NEWS score.

Investigations: FBC, U&E, LFT, Clotting screen; CXR, AXR, Abdominal USS

Signs and symptoms: abdominal pain and distension; dyspnoea; bulging flanks with dullness to percussion; nausea; vomiting; increased fatigue; dyspnoea; decreasing appetite.

Grade 1 (Green)
Asymptomatic; clinical or diagnostic observations only; intervention not indicated.

Grade 2 (Amber)
Symptomatic; medical intervention indicated

Grade 3 (Red)
Severe symptoms; invasive intervention indicated

Grade 4 (Red)
Life threatening consequences; urgent operative intervention indicated

- Check all blood results and act on abnormalities e.g. neutropenia or pancytopenia
- Arrange for elective admission for insertion of ascitic drain under USS control in accordance with local guidelines/practice
- Discuss with Acute Oncology team
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist

- Check all blood results and act on abnormalities e.g. neutropenia or pancytopenia
- Admit as an emergency and arrange for urgent drainage of ascites under USS control
- Plan further management in accordance with trust local guidelines depending upon differential diagnosis
- Discuss with the Acute Oncology team.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 29. CARCINOMATOUS LYMPHANGITIS (Management Pathway)

Carcinomatous lymphangitis refers to a diffuse infiltration and obstruction of the pulmonary parenchymal lymphatic channels. It is associated with many malignancies but 80% are adenocarcinomas, predominantly breast, but also lung, colon and stomach.

Clinical presentation:

Clinically patients present with:

- Increasing breathlessness
- May also have a progressive dry cough or haemoptysis.

Radiation pneumonitis/treatment related pulmonary fibrosis should be considered as can cause similar symptoms.

Diagnosis is based on clinical suspicion in a patient with metastatic cancer and appropriate symptoms.
Chest X-rays can appear normal in 30-50% of cases, but characteristic changes include:

- Bronchovascular markings with irregular outlines
- Reticular-nodular shadowing
- Bilateral lower lobe changes

Other more general changes include:

- Hilar and mediastinal lymphadenopathy
- Pleural effusions.

High resolution CT Scanning is the investigation of choice if CXRs are equivocal or the clinical picture is not obvious.

Treatment:

- Corticosteroids (such as dexamethasone 4mg bd, with appropriate PPI cover and not be taken later than 2pm to avoid insomnia) may be beneficial to aid in the management of the associated dyspnoea.
- Discussion with the patient's oncology team is warranted as to whether there are any systemic oncological treatments available, as treating the malignancy itself is the only long-term option.
- Unfortunately the prognosis of patients who develop carcinomatous lymphangitis is poor, with less than 50% surviving 3 months.

Consider urgent referral to the palliative care team for symptom management and advice.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 30. CENTRAL VENOUS ACCESS DEVICES (CVAD) PROBLEM MANAGEMENT

RISKS AND COMPLICATIONS.

There are several risks and complications related to the insertion and maintenance of CVADs. These are briefly discussed below. If you have any concerns relating to any of the following problems please refer to your Local Management Guidelines or contact your Acute Oncology Team.

Removal of the line is not always necessary; please seek appropriate advice from your Acute Oncology Team or the 24 hour oncology on call rota before removing a line.

Infection

Localized infection: Tunnel infections can occur in skin tunnelled CVADs, around the insertion site of PICCs or in the port pocket. These areas should be examined prior to access and/or daily by HCP or self-monitoring for any signs of redness, swelling or discharge, pain or tenderness at the exit site. (Absence of discharge does not rule out local infection because if a patient is neutropenic, pus may not be produced). If neutrophils are in normal range and the patient is well and apyrexial, localized infection can be treated with oral or intravenous antibiotics according to the clinical condition of the patient at that time. Lack of response to antibiotics should be acted upon quickly so that infection does not progress further.

Luminal infection: Often presents as pyrexia/shivers/rigor following catheter flushing. If untreated this can progress to septicaemia. If a CVAD infection is suspected the patient should be admitted to hospital for blood cultures and intravenous antibiotics. This is a serious complication of CVADs and can be life threatening if the patient has recently received chemotherapy and is neutropenic.

Any heath professional caring for a patient with a CVAD must be able to recognize the signs and symptoms of septicaemia. First dose of antibiotics for patients with neutropenic sepsis should be delivered as per national directives within 1 hour of arrival to hospital to injection time.

Seek advice regarding line removal from the AO Team or Oncology on call rota.

Thrombosis

Thrombosis is the formation of a clot within a blood vessel. Signs and symptoms of thrombosis secondary to CVAD insertion include; pain in the arm, shoulder or chest, swelling, auxiliary blood vessel formation. Thrombosis should be managed according to locally agreed guidelines.

Phlebitis

This is the inflammation of the intima of the vein and it can be mechanical or infective in origin.
Mechanical phlebitis is most common in PICCs and can occur within 72 hours to a week of CVAD insertion.
Signs and symptoms include pain, erythema, warmth, and a venous cord may be palpable. Mechanical phlebitis can be treated effectively with application of heat pads every 4-6 hours for 20 minutes at a time. Patients should also be offered analgesia as required. CVADs should not be removed without seeking appropriate advice from the AOS Team

Haematoma

This results from uncontrolled bleeding around the site of insertion. It is a hard and painful swelling with infiltrated blood. Hirudoid cream can be used to soothe and relieve bruising and haematoma: 5-15cm of cream applied over affected area up to 4 times daily and gently massaged into the skin. Firstly check if the patient is taking any anticoagulant therapy or aspirin. Also check platelet count and clotting.

Catheter Migration

Although secured in place, the catheter tip can migrate from its desired position just above the right atrium. This can be due to the patient being very active, or the catheter not being secured properly or in the case of skin tunnelled catheters poor granulation may result in the Dacron cuff slipping. The sign is that the length of the catheter outside the body gets longer. It is important to always check the length before any manipulation of the catheter. If the Dacron cuff is visible or the length of the PICC is greater outside the body, chest x-ray will be required to confirm the position of the catheter tip. Symptoms of catheter migration can include pain in the neck and a rushing sound in the ear during flushing. Management will depend on tip position but may require removal of device.

Guideline 30 continued. CENTRAL VENOUS ACCESS DEVICES (CVAD) PROBLEM MANAGEMENT RISKS AND COMPLICATIONS.

Air Embolus

This is a very rare complication. Methods to reduce the risk of air embolus should be used when inserting, accessing or removing a CVAD. Only health professionals trained and competent to do so should be inserting, accessing or removing. Local policies should be adhered to. If a patient suddenly becomes acutely short of breathe and distressed, air embolism should be suspected. Check the CVAD for any obvious damage and clamp above if any are apparent. Lay the patient in left lateral Trendelenburg position and call for urgent medical assistance

Catheter Damage

If it is an open-ended catheter that is split above the clamp, use an atraumatic clamp (or clamps covered in gauze) above the damaged area. Apply an occlusive dressing over the split area. Consider repairing the CVAD if appropriate or it may require removal.

Accidental Removal

Arrangements then need to be made for replacement of the CVAD. Inspect the catheter to ensure that it is intact if in doubt then X-ray confirmation is required

Unable to aspirate blood

Patency of CVADs should be established prior to administration of any drug or solution (RCN 2010). This is to ensure that any risk of extravasation is minimized. Occlusion can be termed complete, partial or withdrawal occlusion.
Complete occlusion can be due to a clot or drug precipitation within the line or a fibrin sheath completely enveloping the device. It results in an inability to either withdraw blood or infuse liquids
Partial occlusion can be due to a small blood clot within the catheter or an external obstruction, for example a twist or a kink in the catheter. It results in difficulty withdrawing blood.
Withdrawal occlusion can result from a fibrin tail or malposition of the tip of the catheter and results with inability to withdraw blood but fluids can be administered with ease.
Fibrin sheaths can form as quickly as 24 hours following insertion, fluids can be administered but aspiration of blood is impossible as the fibrin acts as a valve (Amesur 2007).
Consider cathetergram when diagnosing the reason for catheter blockage.

Unblocking Central Venous Catheters

Thrombolytics such as urokinase are used to re-establish patency of CVADs obstructed with intraluminal or extra luminal thrombus or fibrin sheath. This agent breaks down fibrin. Thrombolytics should be prescribed by the medical staff and administered by staff that have been trained to do so, only after other reasons for catheter obstruction have been ruled out.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 31. Cerebral/or CNS oedema and/or cerebral space occupying lesion. (Management Pathway)
Cerebral space occupying lesion – may be primary disease site or metastatic deposits.
Acute cerebral /other CNS oedema – may be disease related e.g. developing around an intrinsic lesion within the brain tissue e g. a tumour or an abscess or treatment related in the patient who is receiving radiotherapy

Identify: Patients who have received/receiving systemic anti-cancer treatment or are at risk of disease related immunosuppression or a history of bone marrow transplant. These patients may be myelosuppressed/ neutropenic and at risk of sepsis. If present, this should be managed according to guidelines.
Observations: Calculate NEWS score.
Investigations: Urgent FBC, U&E, CT scan of head (If CT negative and strong suspicion of brain lesion, due to clinical presentation, consider MRI brain).
Full Clinical / neurological assessment: Signs and symptoms may include new onset of seizures, headache, visual disturbance, nausea and/or vomiting, cognitive dysfunction, confusion, disorientation and/or memory loss, motor dysfunction, symptoms of stroke.
Questions:

- Cancer diagnosis/primary disease/ known metastatic disease
- Currently receiving or have recently completed SACT treatment
- Currently receiving or have recently completed radiotherapy treatment
- Are the presenting symptoms new
- Are there any co-existing conditions such as epilepsy, hypertension or medication that may account for the patients' symptoms?

NOTE: If there is no history of previous malignancy please see MUO/CUP guideline 38 on P49

Grade 1 (Green)
Fully functional status (i.e. able to work) with minor neurologic findings, no medication needed

- Patients should be discussed with either the Acute Oncology Team or on call oncologist as they may require specialist review and management planning prior to discharge.
- Advise to contact the 24 hour advice line if symptoms worsen or persist

Grade 2 (Amber)
Neurologic findings present are sufficient to require home care, nursing assistance may be required. Medications including steroids/anti-seizure agents may be required.

- Commence dexamethasone
- 8-16mg oral OD (IV if required) with PPI cover
- Anti-epileptic medication if having convulsions.
- Admit for monitoring and care.
- Patients should not be discharged until the Acute Oncology Team has reviewed them.
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist

Grade 3 (Red)
Neurologic findings requiring hospitalisation for initial management

Grade 4 (Red)
Serious neurologic impairment which includes paralysis, coma or seizures>3 per week despite medication management - hospitalisation required

- Dexamethasone 16mg oral OD (IV if required) with PPI cover
- Anti-epileptic medication if having convulsions.
- Admit for monitoring, on going assessment and management in accordance with local trust guidelines.
- Early critical care management/advice if deterioration.
- **Note:** need for caution in patients with no previous known malignancy and lymphoma suspected steroids might cause rapid resolution of the tumour, which may make histological diagnosis very difficult. If possible, steroids should be avoided before biopsy if lymphoma suspected. This should also be considered in patients presenting with MSCC

Referral to the Acute Oncology Team is recommended for all patients, immediate advice is available from the Acute Oncology on call rota.
Patients with no known malignancy will require neurosurgical referral
Patients with known primary disease presenting with metastatic disease require referral to the Brain and CNS MDT.
Patients on active anti - cancer treatment will require oncological review prior to further treatment.
Consider palliative care referral in patients with poor performance status, advanced disease, for symptom control advice.

Guideline 32. EXTRAVASATION (Management Pathway)

This is the accidental administration of drugs into the extra vascular tissue instead of into the vein. If the drug extravasated is a vesicant, the damage to the surrounding tissue can be extensive and tissue necrosis can occur.

Extravasation may be linked to peripheral cannulation or a Central Venous Access Device (CVAD).

SUSPECT PERIPHERAL EXTRAVASATION IF:

a) Patient complains of burning or stinging pain at or around cannula site
b) There is evidence of swelling, induration, and leakage at site
c) There is resistance on plunger of syringe or absence of free flow of infusion
d) There is no blood return (if found in isolation via a peripheral cannula this should not be regarded as an indication of a non-patent vein).

Action:

- If extravasation occurs during peripheral administration of SACT**; Act immediately** according to your local extravasation guidelines.
- If a patient presents as an emergency following previous peripheral administration of SACT**;**

Act immediately - Extravasation of a vesicant drug should be treated as an emergency**.** If it is discovered the local Acute Oncology Team should be contacted, if out of hours use the Acute Oncology on call rota contact. The local extravasation policy should be followed, and recommended antidotes should be administered appropriately.

Although administration of drugs via CVADs carry less risk of extravasation than peripheral administration, if it does occur the damage is likely to be larger and more severe than with peripheral administration. This is because the event is not likely to be noticed immediately and delays to the treatment of extravasation result in damage limitation rather than cure.

SUSPECT CVAD EXTRAVASATION IF:

Signs and symptoms include:

- The patient complains of pain around the insertion, along the tunnel or over the port area
- There is evidence of redness and swelling around the insertion, along the tunnel or over the port area
- There is visible leaking of the drug via the skin tunnel or around the exit site.

Extravasation of a vesicant drug should be treated as a medical emergency.

If it is discovered the local Acute Oncology Team should be contacted, if out of hours use the 24 hour telephone on call contact. The local extravasation policy should be followed, and recommended antidotes should be administered appropriately.

IMMEDIATE ACTION FOR ALL DRUG CATEGORIES IF CVAD EXTRAVASATION IS SUSPECTED.

If the patient is receiving an active infusion STOP the infusion immediately

↓

Leave the central venous catheter in place.

↓

Attempt to aspirate as much drug as possible with a new syringe.

↓

For ports, aspirate then remove needle

↓

Inform a senior member of the Acute Oncology Team

↓

Organise X-ray of line or cathetergram

For vesicant extravasations or large volumes of irritant drugs refer to plastic surgeon as soon as possible after detection.

Guideline 33. HYPERCALCAEMIA OF MALIGNANCY (Management Pathway)

Definition: A disorder characterized by laboratory test results that indicate an elevation in the concentration of calcium (corrected for albumin) in blood. **Corrected calcium >3.4mmol/L requires URGENT treatment.**

Questions:

- Is there a cancer diagnosis/primary disease?
- Are they taking anticancer treatment at the moment or recently? If so what treatment and when did it stop?
- Have they previously suffered from hypercalcaemia?
- Are they taking any other medication? (Stop any calcium supplements).

Investigations:

- ECG - look for shortened QT interval or other conduction abnormalities
- Bloods - Calcium adjusted for albumin, Phosphate, PTH, Vitamin D, Urea and electrolytes

Examination:

- Assess for symptoms of hypercalcaemia and duration
- Fluid balance status

Signs /symptoms:

- Polyuria and thirst
- Anorexia
- Nausea/Vomiting
- Constipation
- Abdominal pain
- Fatigue / Lethargy
- Mood disturbance
- Cognitive dysfunction
- Confusion
- Seizures
- Renal impairment
- Pancreatitis
- Peptic ulceration
- Muscle weakness
- Band keratopathy
- Hypertension
- Cardiomyopathy
- Shortened QT interval
- Dysrhythmias
- Coma

Grade 1 (Green)
Corrected serum calcium of >ULN -2.9 mmol/l (ULN = upper limit of normal)

Grade 2 (Amber)
Corrected serum calcium >2.9 - 3.0 mmol/l
Often asymptomatic and does not usually require urgent correction

Grade 3 (Red)
Corrected serum calcium >3.0 - 3.4 mmol/l
May be well tolerated if risen slowly, but may be symptomatic and prompt treatment is usually indicated.

Grade 4 (Red)
Corrected serum calcium >3.4 mmol/l
Requires urgent correction due to the risk of dysrhythmia and coma.

Is patient known to have an active malignancy?

Check FBC, ESR, U&E, LFT, TFT, PTH, cortisol, vitamin D & myeloma screen, start IVI & seek advice from endocrinologist – consider new cancer. Review need for any drugs, which may affect renal blood, flow e.g. NSAIDs, diuretics, ACEIs, ARBs

If **YES** - Is this the first episode of hypercalcaemia?

N

If 1st episode of hypercalcaemia, give 2-4 litres of 0.9% sodium chloride IV followed by zoledronic acid 4mg IV in 100ml 0.9% sodium chloride.
or pamidronate, dose according to corrected calcium.
Seek advice from endocrinologist.
Review need for any drugs, which may affect renal blood, flow e.g. NSAIDs, diuretics, ACEIs, ARBs

If creatinine clearance is <30ml/min (GFR<10), do not give bisphosphonate SEEK ADVICE. Zoledronic acid dose needs to be reduced if renal impairment present.

If 2nd or subsequent episode of hypercalcaemia, give 2-4 litres of 0.9% sodium chloride IV, followed by zoledronic acid 4mg IV in 100ml 0.9% sodium chloride.
Review need for any drugs, which may affect renal blood, flow e.g. NSAIDs, diuretics, ACEIs, ARBs

Recheck U&E & calcium after 4-7 days or sooner if need to monitor fluid replacement.

DO NOT GIVE FURTHER BISPHOSPHONATE UNTIL AT LEAST 4 DAYS AFTER PREVIOUS DOSE
Maximum effect not seen yet – there is a risk of hypocalcaemia if further bisphosphonate given too soon.
If calcium remains elevated **SEEK Endocrinology /oncology ADVICE regarding second line management.**
Check calcium weekly, levels remain high and it is 3 weeks or more since last dose of bisphosphonate, give zoledronic acid 4mg IV; if less than 3 weeks since last dose of bisphosphonate, **SEEK Endocrinology /oncology ADVICE** ***especially if renal impairment present.***

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.endocrineconnections.com/content/5/5/G9.full

Guideline 34. HYPOMAGNESAEMIA (Management Pathway)

A disorder characterised by laboratory test results that indicate a low concentration of magnesium in the blood. Many cancer drugs can lead to hypomagnesaemia for example cisplatin, carboplatin, liposomal doxorubicin, cabozantanib, cetuximab, and panitumumab. Other drugs commonly used in cancer patients, e.g. diuretics, gentamicin and other aminoglycoside antibiotics, can cause or contribute to low magnesium,. Patients with severe treatment related diarrhoea are also at risk. Normal magnesium range = 0.70 – 0.99 mmol/L (Values will be lab assay specific)

Hypomagnesaemia is often detected on blood tests when the patient is being assessed for other reasons therefore most patients are asymptomatic as the levels are only mildly depressed (> 0.50mmol/L).

When serum magnesium levels drop more significantly (< 0.50mmol/L) most patients have non-specific symptoms but they may then go on to develop:

- Cardiac or muscle related symptoms such as weakness, cramping, tachycardia / palpitations.
- Neurological complaints can be that of vertigo, ataxia, depression, and in severe cases seizures or altered mental state.

Investigation: ECG and consider continuous cardiac monitoring. Check potassium levels.

Note: review antiemetics and PPI's as there may be contraindications in patients with low magnesium

Examination Findings

Neuromuscular Irritability: Hyperactive deep tendon reflexes; muscular fibrillation; +ve Trousseau (facial nerve hypersensitivity) & Chvostek (metacarpal hyper flexion) signs; dysarthria or dysphagia secondary to oesophageal dysmotility.

CNS Hyper sensitivity: Irritability and combativeness; disorientation; psychosis; ataxia, vertigo, nystagmus & seizures

Cardiac findings (ECG): Paroxysmal atrial and ventricular dysrhythmias; repolarisation alternans

Grade 1 (Green)	Grade 2 (Amber)	Grade 3 (Red)	Grade 4 (Red)
< LLN - 0.5 mmol/L	< 0.4- 0.5 mmol/L	< 0.3 – 0.4 mmol/L	< 0.3 mmol/L Life threatening consequences
• These patients are typically asymptomatic. • Consider oral Magnesium replacement to avoid a fall to critical levels: Magnaspartate Mag Glycerophosphate (discuss with pharmacy). • Encourage Mg rich diet e.g. spinach, pumpkin seeds, avocado, almonds. figs, swiss chard.	• Consider oral Magnesium replacement to avoid a fall to critical levels: Magnaspartate Mag Glycerophosphate (discuss with pharmacy). • Check bloods in 24- 48 hours. • Correct any other electrolyte imbalance as necessary. • Encourage Mg rich diet e.g. spinach, pumpkin seeds, avocado, almonds. figs, swiss chard.	• Admit for administration of Magnesium Sulfate by intravenous infusion. • Correct any other electrolyte imbalance as necessary • Consider continuous cardiac monitoring	• Admit for administration of Magnesium Sulfate by intravenous infusion. • In severe cases such as cardiac arrhythmias Magnesium Sulfate can be given as a bolus but under HDU / ITU supervision. • Consider continuous cardiac monitoring

https://bnf.nice.org.uk/drug/magnesium-sulfate.html#indicationsAndDoses

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 35. (2 page guideline) Hyponatraemia Management Pathway

Hyponatraemia can be defined as serum sodium <135 mmol/L. The clinical significance of hyponatraemia depends on its severity, its speed of onset and its underlying cause. Severe hyponatraemai can be life threatening.

Initial Assessment

Observations: Calculate NEWS score. Fluid balance.

Investigations: FBC, U&E. Serum Osmality, Glucose, Cortisol, Thyroid Function, LFT.Urine osmolality and Na+

Symptoms:

1. Severe
- Vomiting
- Cardiorespiratory arrest
- Seizures
- Reduced consciousness
- Coma - GCS<8

2. Moderately severe
- Nausea without vomiting
- Confusion
- Headache

3. Mild or absent symptoms

The clinical significance of hyponatraemia depends on its:
- Severity
- Speed of onset
- Underlying cause
- Range and degree disease and of co-morbidities.

Management decisions should be based on presenting clinical symptoms rather than the degree of hyponatraemia.
N.B. Severe symptoms are unlikely with serum sodium >130 mmol/L and alternative causes of neurological dysfunction should be considered in this context.

The decision to treat with hypertonic fluid and supervision of treatment should be the responsibility of a senior clinician with appropriate training and skill.

The aim is to achieve a 5mmol/l rise in serum Na+ within the first hour, reducing immediate danger from cerebral oedema while minimising the risk of over-rapid correction and osmotic demyelination

Mild: 130–135 mmol/L

Moderate: 125 -129 mmol/L

Profound: <125 mmol/L

N.B. The severity of symptoms may not match the degree of hyponatraemia: profound hyponatraemia may be symptom free, while some patients with moderate biochemistry may have significant signs and symptoms.

STEP 1. Patients with severe symptoms require immediate management, irrespective of cause

↓

Within 1st Hour
IV infusion 150 mls of 3% hypertonic saline or equivalent
Over 20 mins in close monitoring environment

↓

Check Na+
IV infusion 150 mls of 3% hypertonic saline or equivalent
Over 20 mins whilst waiting result

↓

Repeat twice or until 5mmol/l increase in Na+

↓

Follow up management after 5mmol/l rise in Na+
Stop infusion hypertonic saline
Keep IV line open with minimal volume 0.9% saline
Start diagnosis –specific management
Limit increase in Na+ to 10mmol in first 24h
Limit increase Na+ to additional 8mmol/l every 24h thereafter until Na+ 130mmol/l
Check Na+ 6h, 12h and daily until stable

STEP 2 recommended approach if no improvement following 5mmol/l rise in Na+ in the first hour

↓

IV infusion 150 mls of 3% hypertonic saline or equivalent
Over 20 mins in close monitoring environment
Aim additional 1mmol/l increase in Na+

↓

Indications for stopping infusion
Symptom improvement
Na+ increases >10mmol/l in total or 130mmol/l (which ever is first)

↓

Explore other causes of symptoms and refer to endocrinology for further advice and guidance.

Differential diagnosis of hyponatraemia following emergency treatment

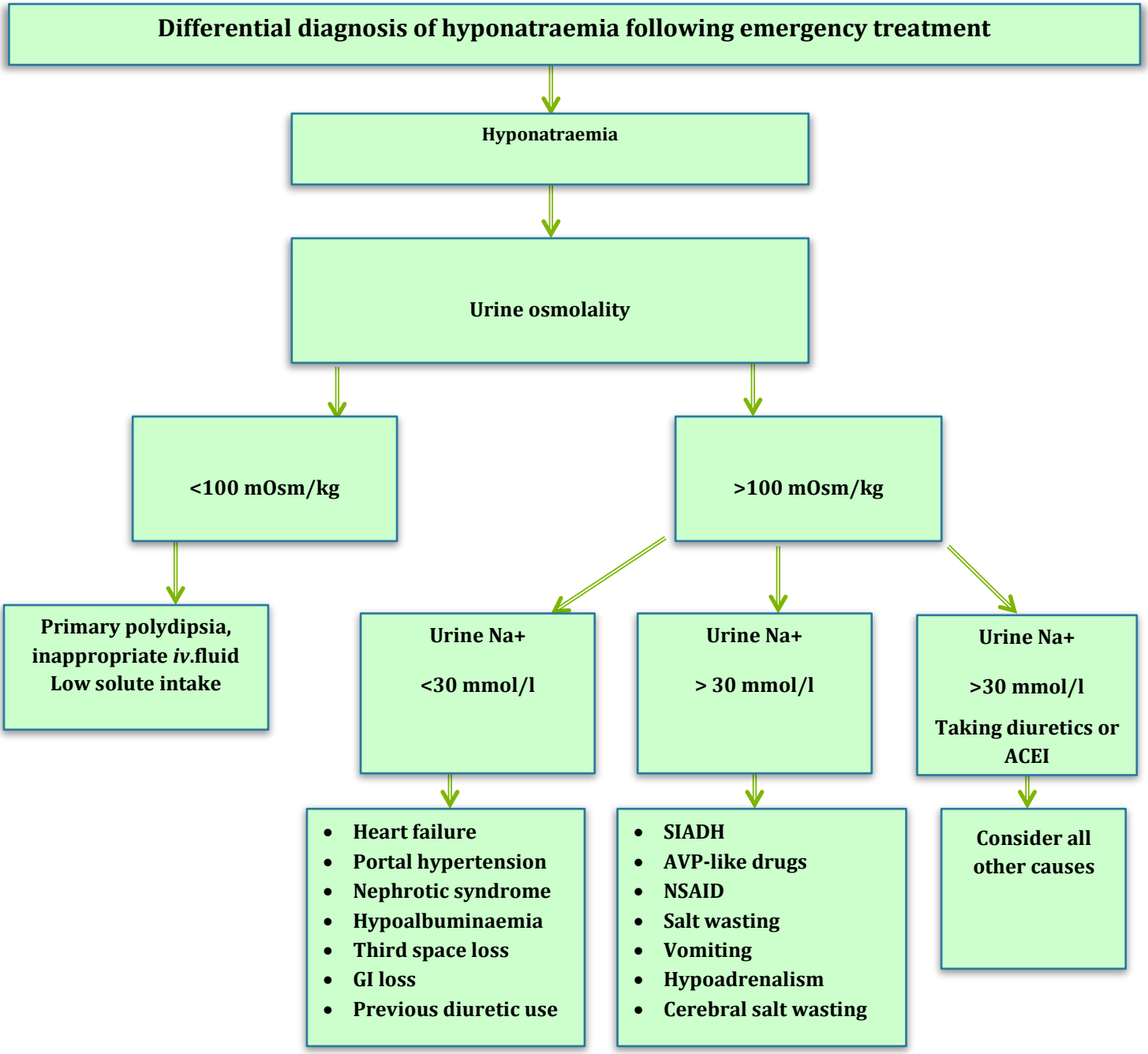
Measurement of urine osmolality and urine Na+ concentration is central to defining the aetiology of hyponatraemia. Please see following page (P46) for further guidance

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.endocrineconnections.com/content/5/5/G4/F3.expansion.html

Guideline 35 continued. Hyponatraemia Differential diagnosis

Hyponatraemia can be defined as serum sodium <135 mmol/L. The clinical significance of hyponatraemia depends on its severity, its speed of onset and its underlying cause. Severe hyponatraemai can be life threatening.



Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.

Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.

WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

http://www.endocrineconnections.com/content/5/5/G4/F3.expansion.html

Guideline 36. MALIGNANT PERICARDIAL EFFUSION (Management Pathway)

An accumulation of fluid within the pericardial sac leading to an effusion can be a presenting symptom in acute oncology patients. Two thirds of cancer patients have subclinical pericardial effusions with no overt cardiovascular signs or symptoms. 50% of cases initially present with symptoms of cardiac tamponade. Symptoms are often attributed to underlying cancers and are often a pre-terminal event; however, prompt diagnosis and management can achieve significant palliation.

Causes

Most malignant pericardial effusions result from direct malignant involvement with the pericardium. Other, rarer causes of effusions in cancer patients include radiation-induced pericarditis or chemotherapy-induced pericarditis associated with agents such as doxorubicin or cyclophosphamide.

Clinical Findings

- Dyspnoea (majority), fatigue, or asthenia may be the initial symptoms.

Other common symptoms include:

- Cough
- Chest pain
- Orthopnoea

On examination, findings include:

- Elevated JVP
- Tachycardia
- Hypotension
- Pulsus paradoxus (an abnormally large decrease in pulse and systolic blood pressure (>20mmHg) with inspiration)
- Kussmauls's sign (increased distension of jugular veins with inspiration)

Diagnosis:

Chest X-ray may show a widened cardiac shadow
Echocardiography shows the size of the effusion and haemodynamic consequence
ECG to investigate small ECG complexes

Questions:

- Cancer diagnosis/primary disease
- Cardinal questions related to breathlessness

Differential diagnosis would include chest infection, pulmonary embolism (PE), disease progression (i.e. consolidation / pleural effusion); ascending aortic aneurysm (due to indwelling intravascular catheter)

Grade 1 (Green)
Small effusion with no haemodynamic consequence

Grade 2 (Amber)
Moderate effusion with no or minimal haemodynamic consequence and good left ventricular function

- Enquire regarding signs of sepsis/productive cough - escalate to Grade 3 Red as appropriate
- Discuss with the Acute Oncology team prior to discharge for ambulatory management.
- Early referral to cardiology for management advice
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen

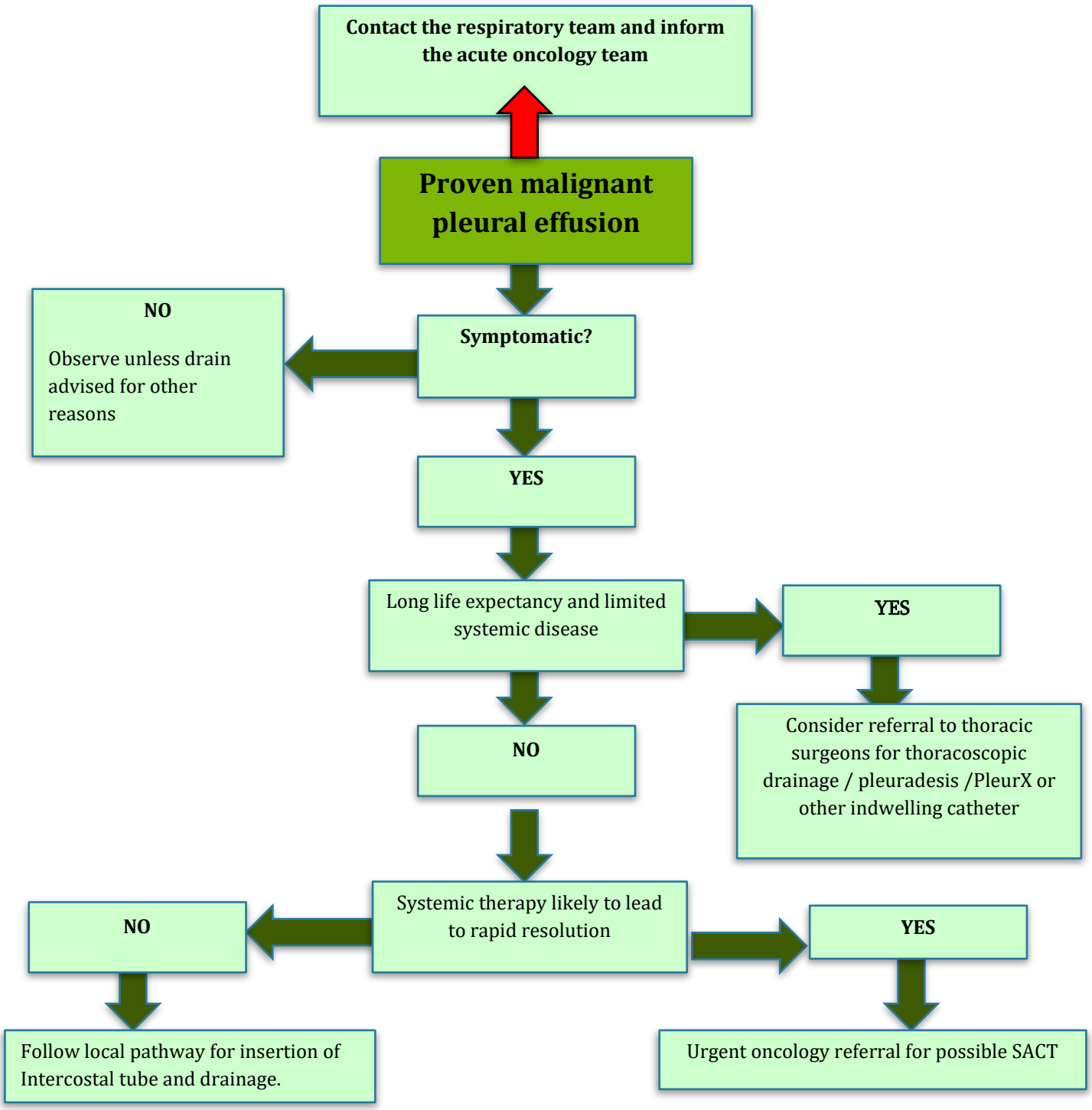
Grade 3 (Red)
Effusion with haemodynamic consequence

Grade 4 (Red)
Cardiac tamponade - life-threatening consequences; urgent intervention required

- Admit patient for on-going assessment, monitoring and symptom management
- Withhold anticoagulation
- Consider immediate therapeutic drainage if cardio-vascular compromise.
- Treatment is best managed with urgent referral to cardiology or cardiothoracic surgical teams – contact SpR on call.
- Inform Acute Oncology Team
- All treatment options should be balanced against the patient's symptoms, overall performance status, level of disease and predicted benefits.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 37. MALIGNANT PLEURAL EFFUSION (Management Pathway)



NOTE: there may be an ambulatory service available locally for the management of stable patients requiring drainage of pleural effusion – contact the respiratory or acute oncology team for advice.

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 38. Malignancy of Unknown Origin (MUO) Cancer of Unknown Primary (CUP) (Management Pathway)
The aim of this pathway is to enable early identification of patients that would benefit from anti-cancer treatment and to prevent unnecessary investigations in those patients who are unfit for treatment or do not wish to proceed with treatment.
https://www.nice.org.uk/Guidance/CG104

Initial Assessment
Observations: Calculate NEWS score.
History: Full history including rate of change of symptoms. Assess and record **current performance status** and co-morbidities.
Assess/establish patients understanding and wishes with regards to investigation and treatment pathway.
Examination: Complete clinical examination (including a breast, PR, PV, testicular and skin examination)
Laboratory Investigations:

- **All patients:** FBC, U&E, LFT, Creatinine, Calcium, LDH, CRP.
- Men with midline disease /brain metastases: Serum αFP and βhCG
- Women with pelvic or peritoneal disease: CA125
- Men with bone metastases: PSA
- Patients with liver only disease: αFP
- Consider myeloma screen - for bone lesion seen on scan with no obvious primary – immunoglobulins/electrophoresis, serum free light chains and urine for bence jones protein
- If FBC is abnormal – request blood film which may demonstrate a haematological malignancy such as lymphoma/leukaemia or suggest the possibility of bone marrow metastases
- Urinalysis for blood
- Patients with altered bowel habit: consider CEA

Note: other tumour markers are generally not useful in diagnosis
Imaging:

- CT thorax, abdomen and pelvis is the staging investigation of choice in most circumstances
- Other investigations (including endoscopies) only as indicated by signs and symptoms

Imaging:

- Patients with a solitary metastasis should be referred to the appropriate specialist team *before* biopsy
- All other patients, assess fitness and suitability for biopsy to establish histology to guide future treatment
- Detailed clinical information on the request form is essential

Further management:

- **Discuss with the Acute Oncology Team**
- If clinical, radiological and pathological findings suggest a specific cancer primary refer to relevant MDT (please see guidance below)
- Otherwise refer to **unknown primary MDT and/ or Acute Oncology Team (consider local protocol).**
- Please ensure patient is informed of results and plan for onward referral –some patients may be managed as outpatients if the appropriate infrastructure is in place
- **Early** referral to **palliative care** for advice on symptom management and continuing care should be considered where appropriate

Patterns of disease requiring URGENT specific action:
Spinal cord compression **– urgent admission and referral to acute oncology team and/or spinal cord co-ordinator**
Men with midline disease **– urgent referral to oncology (? germ cell)**
Superior Vena Cava Obstruction - **urgent referral to lung MDT for consideration of stent**
Suspected lymphoma, myeloma, plasmacytoma – **urgent referral to haematology**

Patterns of disease requiring specific action:
Men with bone metastasis and elevated PSA – referral to urology MDT
Women with axillary nodes – referral to breast surgeons/ MDT
Women with peritoneal disease – referral to gynaecology /MDT, unless histology suggests non gynaecology origin
Solitary liver lesion – requires referral to hepatobiliary MDT
Neck nodes – requires referral to head and neck or neck nodes clinic as appropriate locally
Isolated brain metastasis – requires referral to neurology MDT

Always make sure that the Acute Oncology Team are informed of patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology on call rota.

Guideline 39. PNEUMONITIS - Radiation or chemotherapy induced (Management Pathway)

Definition: A disorder characterized by inflammation focally or diffusely affecting the lung parenchyma

Signs and symptoms of radiation or chemotherapy induced pneumonitis

Clinical pneumonitis, or inflammation of the lung(s), can often display non-specific signs.

These can include:

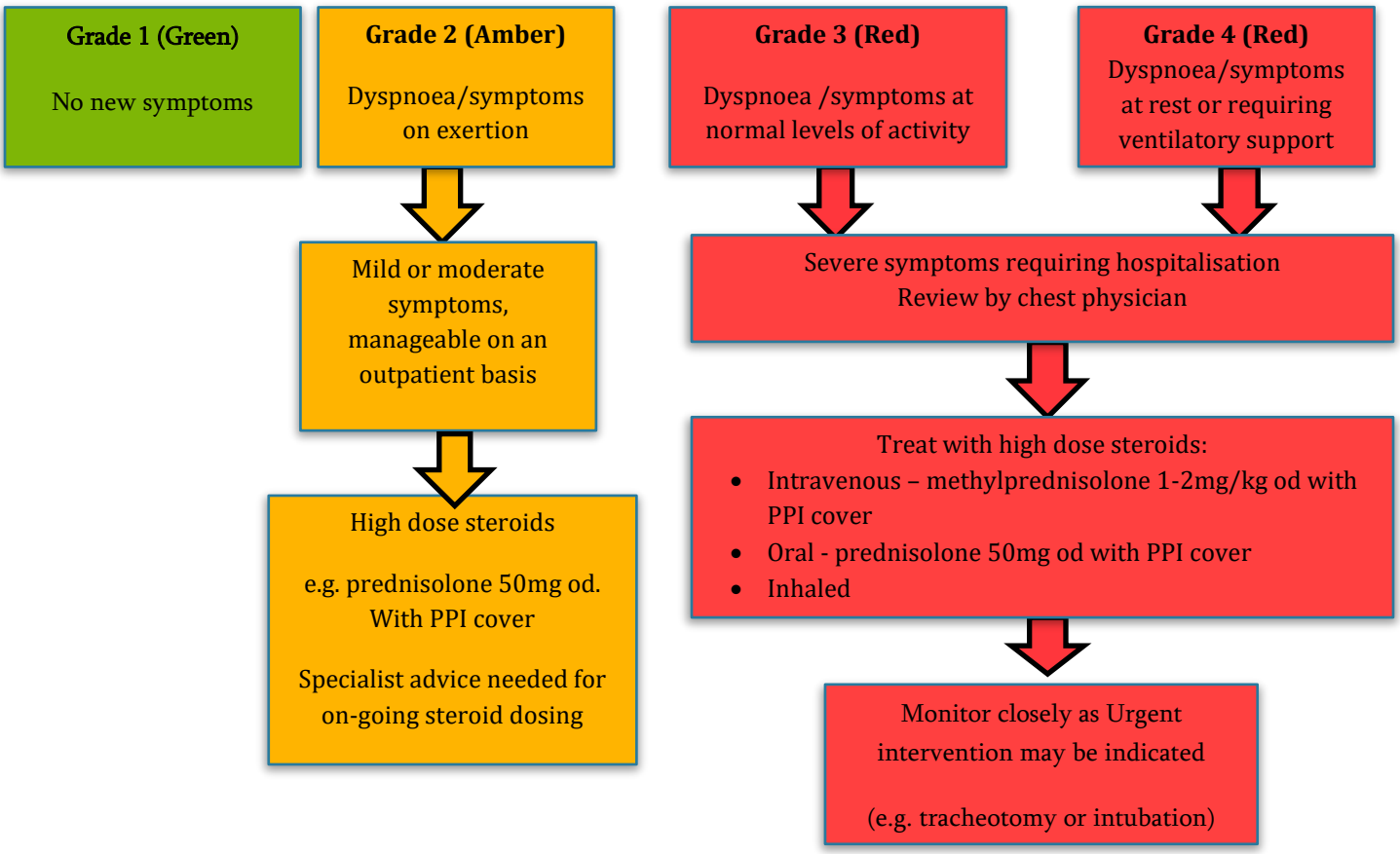
- Mild hypoxia
- Pleural rub/effusion
- Fine crepitations – widespread if drug induced, localised if following focal radiation
- Low grade fever
- The development of acute or sub acute dyspnoea, which after history and examination does not reveal pneumonia, tumour recurrence, or any other specific aetiology
- In addition to dyspnoea, there may be a new or worsening cough

Clinical radiation pneumonitis may develop in 20% of lung carcinoma patients:

- The median time to onset of symptoms is 3 weeks after radiation therapy (but may be up to 3 months)

Initial Assessment:

- Clinical evaluation, history, physical examination and review of observations
- Chest X-ray
- Calculation of Wells score
- CT (high resolution and CTPA) to exclude cancer progression and pulmonary embolus



Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Guideline 40. SUPERIOR VENA CAVA OBSTRUCTION (SVCO) (Management Pathway)
SVCO is an obstructive emergency that may occur as the result of progression of a malignancy or may be the diagnostic symptom. SVCO is caused by external pressure, thrombus or direct tumour invasion causing obstruction of the superior vena cava and occurs in 3-8% of patients with cancer.

Questions:
- Cancer diagnosis/primary disease
- Cardinal questions related to breathlessness
- Differential diagnosis would include Chest infection, pulmonary embolism (PE), disease progression (i.e. consolidation / pleural effusion); ascending aortic aneurysm (due to indwelling intravascular catheter)

Signs and symptoms:
- Dyspnoea
- Headaches
- Chest pain
- Stridor- due to laryngeal oedema
- Dilated anterior chest wall veins
- Swelling of face and neck
- Non-pulsatile JVP
- Confusion
- Coma

Investigations: CTPA to define tumour extent, site of occlusion or stenosis and extent of any thrombus. SVCO can be an incidental finding on CT.
Seek advice from the Acute Oncology and/or the Respiratory team as soon as possible to guide investigations and management.

Grade 1 (Green)
Oedema in head or neck Vascular distension, cyanosis; plethora

Grade 2 (Amber)
Oedema in head or neck with functional impairment (mild dysphagia, cough, visual disturbances)

Grade 3 (Red)
Mild or moderate cerebral oedema (headache, dizziness) or mild/moderate laryngeal oedema or diminished cardiac reserve (syncope after bending)

Grade 4 (Red)
Significant cerebral oedema (confusion) or significant laryngeal oedema (stridor) or significant haemodynamic compromise

- Enquire regarding signs of sepsis/productive cough - escalate to Grade 3 Red as appropriate
- Consider steroid therapy to manage symptoms of oedema and prevent deterioration
- Enquire if history of underlying chest complaints e.g. asthma, COPD – advise patients around usual management of exacerbations advise to discuss with GP or other associated health professional managing this condition.
- Discuss with the Acute Oncology team – arrange urgent oncology and/or respiratory review
- Telephone/review patient within 24 hours and ask patient to contact the 24-hour advice line if symptoms worsen or persist

- Admit for further assessment and on-going management
- Monitor for evidence of:
  - Desaturation
  - Infection
  - SACT/chemotherapy toxicities
  - Haemodynamic compromise
- Address life threatening symptoms e.g. stridor
- Treatment initially aimed at symptom management
- Commence high dose steroids + PPI – if not contraindicated
- **Seek Urgent Advice from the Acute Oncology and/or the Respiratory team to guide investigations and management.**

Manage in accordance with trust local guidelines depending upon differential diagnosis and clinical status.
Further management may include:

- Stent insertion – performance status
- Chemotherapy – performance status
- Radiotherapy – any contraindications e.g. previous radiotherapy to chest. Inability to lie flat.
- **If thrombus is present consider anticoagulation if no contraindications**

Inform the Acute Oncology Team of the patients' assessment and/or admission as soon as possible.
Immediate advice is available from the Acute Oncology Service or the 24 Hour Oncology on call rota.
WITHHOLD! SACT, including oral therapy until, you have discussed with the Acute Oncology or Site Specific Team.

Glossary

ABCDE approach	Airway,Breathing ,Circulation Disability and Exposure	**ABG**	Arterial Blood Gas
ACE-inhibitors	Angiotensin-converting enzyme inhibitors	**ACTH**	Adrenocorticotropic hormone
ABX	Antibiotics	**ADL**	Activities of daily living
AKI	Acute kidney injury	**ALT**	Alanine aminotransferase
anti-TPO Ab	Antithyroid Peroxidase Antibody	**Anti-Xa l**	Anti–factor Xa assay
APTT	Actvated Partial Thromboplastin Time	**ARDS**	Acute Respiratory Distress Syndrome
AST	Aspartate aminotransferase	**BRAF**	BRAF is a human gene that encodes a protein called B-Raf.
BSA	Body surface area	**Ca^{2}+**	
CEA	Carcinoembryonic antigen	**CDT screen**	Connective Tissue Disease
CK	Creatine Kinase	**CLL**	Chronic lymphocytic leukaemia
CMV	Cytomegalovirus	**COPD**	Chronic obstructive pulmonary disease
CRP	C-Reactive Protein Test	**C&S**	Culture and sensitivity
CTPA	Computed tomography pulmonary angiography	**CVAD**	Central Venous Access Device
CXR	Chest X-ray	**DIC**	Disseminated intravascular coagulation
DNACPR	Do Not Attempt Cardiopulmonary Resuscitation	**DPD deficiency**	Dihydropyrimidine dehydrogenase deficiency
DVT	Deep vein thrombosis	**EBV**	Epstein- Barr virus
ECG	Electrocardiogram	**EGFR antagonists**	Epidermal growth factor receptor antagonists
EMG	Electromyography	**ESR**	Erythrocyte sedimentation rate
FBC	Full Blood Count	**Free T4,**	Free thyroxine 4
Free T3	Free Thyroxine 3	**FSH**	Follicle stimulating hormone
gGT	Gamma-glutamyl transferase	**GCSF**	Granulocyte-colony stimulating factor
GI	Gastrointestinal	**HSV**	Herpes simplex virus
HbA1c	Haemoglobin A1c	**HDU**	High dependency unit
ICPi	Immune checkpoint inhibitors	**IGF-1**	Insulin-like growth factor
INR	International normalised ratio	**irAE**	Immune-Related Adverse Event

ITP	Idiopathic thrombocytopenic purpura	**ITU**	Intensive therapy unit
JVP	Jugular venous pressure	**LDH**	Lactate dehydrogenase enzyme
LH	Luteinizing hormone	**LLN**	Lower limit of normal
LMWH	Low molecular weight heparin	**MEK inhibitors**	Mitogen-activated protein kinase enzymes
MMF	Mycophenolate mofetil	**MRA**	Magnetic resonance angiography
MRI	Magnetic Resonance Imaging	**MSCC**	Metastatic spinal cord compression
MTOR inhibitors	Mammalian Target of Rapamycin Inhibitors	**NEWS**	National Early Warning Score
NSAIDs	Non-steroidal Anti-inflammataory Drugs	**PE**	Pulmonary embolism
PJC	Premature Junctional Complex	**PJP**	Pneumocystis Jiroveci Pneumonia
PPE	Palmar-plantar erythrodysesthesia	**PPI**	Proton pump inhibitor
PR	Per rectum	**PSA**	Prostate-specific antigen
SACT	Systemic Anti-Cancer Therapy	**SALT**	Speech and language therapy
SOB	Shortness of breath	**SVCO**	Superior vena cava obstruction
TKI	Tyrosine kinase inhibitor	**TSH**	Thyroid stimulating hormone
U&E	Urea and Electrolytes	**ULN**	Upper limit of normal
VTE	Venous thromboembolism	**VQ**	Ventilation–perfusion scan
5FU	Fluorouracil		

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ONCOLOGY/HAEMATOLOGY ADVICE LINE

TRIAGE TOOL, VERSION 2 (NOVEMBER 2016)

All Green = self care advice | 1 Amber = review within 24 hours | 2 or more amber = escalate to red | Red = attend for assessment as soon as possible

Patients may present with problems other than those listed below, these would be captured as "other" on the log sheet checklist. Practitioners are advised to refer to the NCI-CTCAE common toxicity criteria V4.03 to assess the severity of the problem and/or seek further clinical advice regarding management.

CAUTION! Please note patients who are receiving or have received **IMMUNOTHERAPY** may present with treatment related problems at anytime during treatment or up to 12 months afterwards. If you are unsure about the patient's regimen, be cautious and follow triage symptom assessment.

Toxicity/Symptom	0	1	2	3	4
Fever - receiving or has received Systemic Anti Cancer Treatment (SACT) within the last 6-8 weeks or immunocompromised.	None.	**IF TEMPERATURE 37.5'c or ABOVE or BELOW 36.0'c or GENERALLY UNWELL - URGENT assessment and medical review - Follow neutropenia pathway. ALERT - patients who have taken analgesia or steroids or who may be dehydrated may not present with an abnormal temperature but may still have an infection and be at risk of sepsis - if in doubt do a count.**			
Chest pain STOP oral and intravenous Systemic Anti Cancer Treatment until reviewed by oncology or haematology team.	None.	**Advise URGENT A&E for medical assessment- 999 NB if infusional SACT in place arrange for disconnection.**			
Dyspnoea/shortness of breath Is this a new symptom? How long for? Is it getting worse? Do you have a cough? How long for? Is it productive? If yes, what colour is your phlegm/spit? Is there any chest pain or tightness? - If yes refer to chest pain Consider: SVCO / Anaemia / Pulmonary embolism / Pneumonitis / Infection.	None or no change from normal.	New onset shortness of breath with moderate exertion.	New onset shortness of breath with minimal exertion.	Shortness of breath at rest.	Life threatening symptoms.
Performance Status Has there been a recent change in performance status?	No change to pre-treatment normal - or fully active,able to carry on all pre-disease performance without restriction.	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, such as light housework or office work.	Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours.	Capable of only limited self care, confined to bed or chair for more than 50% of waking hours.	Completely disabled. Cannot carry out any self care. Totally confined to bed or chair.
Diarrhoea How many days has this occurred for? How many times in a 24 hour period? Is there any abdominal pain or discomfort? Is there any blood or mucus in the stool? Has the patient taken any antidiarrhoeal medication? Is there any change in urine output? Is the patient drinking and eating normally? Consider: Infection / Colitis / Constipation. N.B. Patients receiving immunotherapy or Capecitabine should be managed according to the drug specific pathway and assessment arranged as required.	None or no change from normal.	Increase of up to 3 bowel movements a day over pre-treatment normal or mild increase in ostomy output. Drink more fluids Obtain stool sample. Commence regimen specific antidiarrhoeal.	Increase of up to 4-6 episodes a day or moderate increase in ostomy output or nocturnal movement or moderate cramping. Drink plenty of fluids Obtain stool sample. Commence regimen specific antidiarrhoeal. If diarrhoea persists after taking regimen specific antidiarrhoeal escalate to red. If patient is or has been on immunotherapy escalate to red →	Increase of up to 7-9 episodes a day or severe increase in ostomy output or incontinence / severe cramping /bloody diarrhoea.	Increase>10 episodes a day or grossly bloody diarrhoea.
Constipation How long since bowels opened? What is normal? Is there any abdominal pain and/or vomiting? Has the patient taken any medication? Assess the patients urinary output and colour.	None or no change from normal.	Mild - no bowel movement for 24 hours over pre-treatment normal. Dietary advice, increase fluid intake, review supportive medications.	Moderate - no bowel movement for 48 hours over pre-treatment normal. If associated with pain / vomiting move to red. Review fluid and dietary intake. Recommend a laxative.	Severe - no bowel movement for 72 hours over pre-treatment normal.	No bowel movement for >96 hours - consider paralytic ileus.
Urinary Disorder Are you passing urine normally? Is this a new problem or is this normal for you? Is there any change in the urine colour? Is there any blood in the urine? Is there any incontinence, frequency or urgency? Are you passing your normal amount? Are you drinking normally, are you thirsty? Consider: Infection	None or no change from normal.	Mild symptoms. Minimal increase in frequency, urgency, dysuria nocturia. Slight reduction in output. Drink more fluids. Obtain urine sample for analysis.	Moderate symptoms. Moderate increase in frequency, urgency, dysuria nocturia. Moderate reduction in output. Drink more fluids. Obtain urine sample for analysis.	Severe symptoms. Possible obstruction/retention New incontinence New or increasing haematuria Severe reduction in output	Little or no urine output.
Fever **NOT** receiving Systemic Anti Cancer Treatment (SACT) and **NOT** at risk of immunosuppression.	Normal.		< 36.0'c or > 37.5'c - 38.0'c	>38.0'c - 40.0'c	> 40.0'c
Infection Has the patient taken their temperature? If so when? What is it? - If pyrexial see fever toxicity. Are there any specific symptoms, such as: • pain, burning / stinging or difficulty passing urine? • cough, any sputum, if so what colour? • any shivering, chills or shaking episodes?	None.	Localised signs of infection otherwise generally well.	Signs of infection and generally unwell. * If on active SACT treatment follow neutropenic sepsis pathway. * If not on active treatment arrange urgent local review.	Signs of severe symptomatic infection.	Life threatening sepsis.
Nausea How many days? What is the patient's oral intake? Is the patient taking antiemetics as prescribed? Assess patient's urinary output and colour.	None.	Able to eat/drink reasonable intake. Review anti emetics according to local policy.	Able to eat/drink but intake is significantly decreased. Review anti emetics according to local policy.	No significant intake.	
Vomiting How many days? How many episodes? What is the patient's oral intake? Is there any constipation or diarrhoea? - If yes see specific toxicity. Assess patient's urinary output and colour	None.	1-2 episodes in 24 hours. Review anti emetics according to local policy.	3-5 episodes in 24 hours. Review anti emetics according to local policy.	6-10 episodes in 24 hours.	>10 episodes in 24 hours.
Oral / stomatitis How many days? Are there any mouth ulcers? Is there evidence of infection? Are they able to eat and drink? Assess patient's urinary output and colour.	None.	Painless ulcers and/or erythema, mild soreness but able to eat and drink normally. Use mouthwash as directed.	Painful ulcers and/or erythema, mild soreness but able to eat and drink normally. Continue with mouthwash as directed, drink plenty of fluids. Use painkillers either as a tablet or mouthwash.	Painful erythema, difficulty eating and drinking.	Significant pain, minimal intake and/or reduced urinary output.
Anorexia What is appetite like? Has this recently changed? Any recent weight loss? Any contributory factors, such as dehydration, nausea, vomiting, mucositis, diarrhoea or constipation - If yes refer to specific problem/symptom.	None or no change from normal.	Loss of appetite without alteration in eating habits. Dietary advice.	Oral intake altered without significant weight loss or malnutrition. Dietary advice.	Oral intake altered in association with significant weight loss/malnutrition.	Life threatening complications, such as collapse.
Pain Is it a new problem? Where is it? How long have you had it? Have you taken any pain killers? Is there any swelling or redness? If pain associated with swelling or redness consider **thrombosis or cellulitis**. Back pain consider **metastatic spinal cord compression (MSCC).**	None or no change from normal.	Mild pain not interfering with daily activities. Advise appropriate analgesia.	Moderate pain interfering with daily activities. Advise appropriate analgesia.	Severe pain interfering with daily activities.	Severe disabling pain.
Neurosensory / motor When did the problem start? Is it continuous? Is it getting worse? Is it affecting mobility/function? Any perineal or buttock numbness (Saddle paresthesia)? Any constipation? Any urinary or faecal incontinence? Any visual disturbances? Is there any pain? If yes refer to specific problem / symptom. **Consider** - Metastatic spinal cord compression, cerebral metastases or cerebral event.	None or no change from normal.	Mild paresthesia, subjective weakness. No loss of function. Contact the advice line immediately if deterioration.	Mild or moderate sensory loss, moderate paresthesia, mild weakness with no loss of function.	Severe sensory loss, paresthesia or weakness that interferes with function.	Paralysis.
Confusion/cognitive disturbance Is this a new symptom? How long have you had this symptom? Is it getting worse? Is it constant? Any recent change in medication?	None or no change from normal.	Mild disorientation not interfering with activities of daily living. Slight decrease in level of alertness.	Moderate cognitive disability and/or disorientation limiting activities of daily living.	Severe cognitive disability and/or severe confusion; severely limiting activities of daily living. Altered level of consciousness. **999 - Urgent assessment in A&E.**	Life threatening consequences. Loss of consciousness/unrousable. **999 - Urgent assessment in A&E.**
Fatigue Is this a new problem? Is it getting worse? How many days? Any other associated symptoms? Do you feel exhausted?	None or no change from normal.	Increased fatigue but not affecting normal level of activity. Rest accompanied with intermittent mild activity / exercise.	Moderate or interfering with some normal activities.	Severe or loss of ability to perform some activities.	Bedridden or disabling.
Rash Where is it? Is it localised or generalised? How long have you had it? Is it getting worse? Is it itchy? Are you feeling generally unwell? Any signs of infection, such as pus, pyrexia Moderate = 10-30% of the body surface area (BSA) Severe = greater than 30% of the body surface area (BSA) NB Haematology, follow local guidelines.	None or no change from normal.	Rash covering <10% BSA with or without symptoms, such as pruritus, burning, tightness.	Rash covering 10 - 30% BSA that is limiting normal activities of daily living with or without symptoms, such as pruritus, burning, tightness. Or bleeding with trauma or signs of associated infection.	Rash covering >30% BSA with or without associated symptoms; limiting self care activities. Spontaneous bleeding or signs of associated infection.	
Bleeding Is it a new problem? Is it continuous? What amount? Where from? Are you taking anticoagulants? NB Haematology, follow local guidelines.	None or no change from normal.	Mild, self limited controlled by conservative measures. Consider arranging a full blood count.	Moderate bleeding. **999 - Urgent assessment in A&E.**	Severe bleeding **999 - Urgent assessment in A&E.**	Massive bleed. **999 - Urgent assessment in A&E.**
Bruising Is it a new problem? Is it localised or generalised? Is there any trauma involved?	None or no change from normal.	Localised - single bruise in only one area.	Multiple sites of bruising or one large site.		
Ocular/eye problems Is this a new problem? Any associated pain? Any visual disturbance? Any discharge/sticky eyes?	None or no change from normal.	Mild symptoms not interfering with function.	Moderate to severe symptoms interfering with function and/or any visual disturbance.		
Palmar Plantar syndrome If on active oral SACT therapies follow drug specific pathways. Drug may need to be suspended and medical review arranged.	None.	Mild numbness, tingling, swelling of hands and/or feet with or without pain or redness. Rest hands and feet, use emollient cream.	Painful redness and/or swelling of hands and/or feet. Follow drug specific pathway - may require dose reduction or treatment deferral. Advise painkillers.	Moist desquamation, ulceration, blistering and severe pain. Follow drug specific pathway - arrange urgent appointment for review by specialist team within 24 hours. May require dose reduction or treatment deferral. Advise painkillers.	
Extravasation Any problems after administration of treatment? When did the problem start? Is the problem around or along the injection site? Has the patient got a central line in place? Describe the problem.	None.	Non Vesicant. Review the next day.	Vesicant or drug not known. Arrange urgent review.		

Appendix 1. UKONS 24-Hour Triage Tool – Log Sheet also available at http://ukons.org/index.php/reports/P6

HOSPITAL NAME / DEPT:

UKONS 24 HOUR TRIAGE LOG SHEET (V2 2016)

Patient Details	Patient History	Enquiry Details
Name: Hospital no..... DOB..... Tel no.....	Diagnosis: Male ☐ Female ☐ Consultant..... Has the caller contacted the advice line previously Yes ☐ No ☐	Date..... Time..... Who is calling? ..... Contact no..... Drop in Yes ☐ No ☐

Reason for call
(in patients own words)

Is the patient on active treatment? SACT ☐ Immunotherapy ☐ Radiotherapy ☐ Other ☐ Supportive ☐ No ☐

State regimen..... Are they part of a clinical trial Yes ☐ No ☐

When did the patient last receive treatment? 1-7 days ☐ 8-14 days ☐ 15-28 days ☐ Over 4 weeks ☐

What is the patient's temperature? ☐ °C (Please note that hypothermia is a significant indicator of sepsis)

Has the patient taken any anti-pyretic medication in the previous 4-6 hours Yes ☐ No ☐

Does the patient have a central line? Yes ☐ No ☐ Infusional pump in situ Yes ☐ No ☐

CAUTION! Please note patients who are receiving or have received **IMMUNOTHERAPY** may present with treatment related problems at anytime during treatment or up to 12 months afterwards. If you are unsure about the patient's regimen, be cautious and follow triage symptom assessment.

Advise	24 hour follow up	Assess
Remember: two ambers equal red!		
Fever - on SACT		
Chest Pain		
Dyspnoea/shortness of breath		
Performance Status		
Diarrhoea		
Constipation		
Urinary disorder		
Fever		
Infection		
Nausea		
Vomiting		
Oral/stomatitis		
Anorexia		
Pain		
Neurosensory/motor		
Confusion/cognitive disturbance		
Fatigue		
Rash		
Bleeding		
Bruising		
Ocular/eye problems		
Palmar Plantar syndrome		
Extravasation		
Other, please state:		

Significant medical history

Current medication

Action Taken

Attending for assessment, receiving team contacted Yes ☐ No ☐

Triage practitioner

Signature..... Print..... Designation..... Date / /

Follow Up Action Taken:

Consultants team contacted Yes ☐ No ☐ Date / /

Signature..... Print..... Designation..... Date / / Time: