000 – GUIDELINES FOR THE MANAGEMENT OF SYSTEMIC ANTI-CANCER THERAPY REACTIONS IN ADULTS

Broad Recommendations / Summary

These guidelines are to help practitioners prevent, recognise and successfully treat the incidence of reaction/anaphylaxis from systemic anti-cancer therapy.

The guidelines have been adapted from the former North East Yorkshire and Humber Clinical Alliance (Cancer) NEYHCA CEG – Guidelines for the Management of Chemotherapy Induced Anaphylaxis in Adults, version 2.2a January (2014) - formally HYCCN. NEYHCA has since ceased to exist as has administration or version control facilitation. Therefore, the adapted, updated guidelines are to rebrand and publish directly onto the local HEY Trust Intranet Site and linked to the Queens Centre for Oncology and Haematology; Cancer Services and Chemotherapy CNS Team Website to ensure up to date best practice.

Previous terminology relating to cytotoxic chemotherapy is now under the contemporary term of Chemobiological Systemic Anti-Cancer Therapy, referred to as SACT within the text and includes all classifications of intravenous anti-cancer agents including biological, immunological and hormone therapies in line with up to date evidence and classifications.

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1 PURPOSE / LEGAL REQUIREMENTS / BACKGROUND

The purpose of these guidelines is to inform all Health Care Professionals (HCP) of their responsibility to avoid, recognise and successfully manage the incidence of reaction/anaphylaxis during Chemobiological systemic anti-cancer therapy (SACT).

It remains the responsibility of the practitioner to interpret the application of the guidelines, be aware of best possible practice whilst taking account of local circumstances and the needs and wishes of individual patients.

In reviewing the summary guidelines, local clinicians and managers will be required to assess whether the guidance can be met, and if not what service developments need to be undertaken to achieve the ideal service as defined by the available evidence.

2 POLICY / PROCEDURE / GUIDELINE DETAILS

These guidelines will address:

2.1 Definition of anaphylaxis/anaphylactoid reaction
2.2 Risk factors
2.3 Recognition
2.4 Management and Treatment
2.5 Documentation

2.1 Definition

Anaphylaxis is a hypersensitivity reaction to a stimulant or antigen (i.e. Wasp stings, food allergy, drugs etc.) that occurs in a previously sensitized person. It happens when the body's immune system is over stimulated, resulting in the formation of antibodies which attach to mast cells and basophils. As long as these antibodies remain attached the patient is at risk of a reaction if the antigen is reintroduced into the body. (Allwood et al, 2002).

Anaphylactoid reactions produce the same clinical symptoms as anaphylaxis, but, the mechanism is different. They occur after the first injection of certain drugs and are due to a dose-related pharmacologically induced mediator rather than an immunological one (Page et al, 2002).

The Resuscitation Council, U.K. (2008) has produced a broad consensus regarding appropriate emergency management of acute anaphylactic reactions:
"There is no universally accepted definitions of anaphylactic and anaphylactoid reactions. The term anaphylaxis is usually used for hypersensitivity reactions typically mediated by immunoglobulin (IgE). They occur following earlier sensitization to an antigen and are due to the production of specific (IgE) antibodies in response to the now recognized antigen.
Anaphylactoid reactions (are similar), but do not depend upon hypersensitivity. They occur via direct stimulation of mast cells and basophils, without prior drug exposure.
The term anaphylaxis is referred to encompassing both types of reactions, as manifestations and management are similar, distinction only being of more importance during follow up management.
(Mistovich, 2008)

2.2 Risk Factors

The degree of risk and type of reactions are variable (from mild to life threatening). The onset is more rapid and reaction more often severe from the intravenous (I.V.) route.
Progress may be rapid, slow, or biphasic (more rarely delayed by a few hours or persisting for more than 24 hours).

Adrenaline is generally regarded as the most important drug for any severe anaphylactic reaction. As an alpha-receptor agonist, it reverses peripheral vasodilatation and reduces oedema. The beta-receptor activity dilates the airways, increases the force of myocardial contraction and suppresses histamine and leukotrienes release (The Resuscitation Council, U.K. 2008).

Caution
Intravenous adrenaline should only be administered in special circumstances by medically qualified personnel who have experience of it and are aware of the hazards associated with its use.

For anaphylaxis the recommended dose of adrenaline is used in a dilution of 1:1000 intramuscularly (Fisher, 1995) & The Resuscitation Council, U.K. 2008).

Care needs to be taken if the patient is taking tricyclic antidepressants, monoamine oxidase inhibitors or beta-blockers as they may increase the severity of the reaction and antagonise the response to adrenaline (BNF 2016).

2.3 Recognition

All systemic anti-cancer drugs (as with any other drugs) have the potential to cause allergic (hypersensitivity) / anaphylactic reactions.

The nurse administering systemic anti-cancer therapy must be aware of the signs and symptoms of anaphylaxis and hypersensitivity reactions. This will allow early detection and treatment thus improving the outcome and minimising detrimental effects.

Anaphylaxis does need to be distinguished from other medical conditions that may have some similar symptoms.
There may be difficulty diagnosing anaphylaxis in a patient who is prone to panic attacks. Possible symptoms of panic attack include a sense of anxiety and breathlessness leading to hyperventilation. It does not usually include pallor, wheeze, rash or swelling. Blood pressure (BP) is not affected.
Using the Airway, Breathing, Circulation, Disability, and Exposure (ABCDE) approach will help with treating the differential diagnoses (The Resuscitation Council, U.K. 2008)

All intravenous systemic anticancer therapies are associated with a risk for infusion reactions, which can be unpredictable (Vogel, 2009) and anaphylaxis is always a concern especially when the administered agents are designed to stimulate or potentiate the immune function.

The decision to restart an infusion following a hypersensitivity reaction will depend on the severity of the reaction and discretion of the treating clinician.
Prior to restarting, consider methods to minimise hypersensitivity as follows:

- Inform and instruct patient and family about the possibility and symptoms of hypersensitivity, informing them of action to be taken
- Monitor vital signs
- Consider pre-medication with hydrocortisone and antihistamines.
- Reduce the infusion rate and administer over a longer period of time.
- Alteration of subsequent infusion rates may be undertaken if initial dose is well tolerated, according to manufacturer's guidelines.

Presenting Signs & Symptoms
Taken from the Resuscitation Council (UK) Guidelines 2008.
A diagnosis of anaphylactic reaction is likely if a patient who is exposed to a trigger (allergen) develops a sudden illness (usually within minutes of exposure) with rapidly progressing skin changes and life-threatening airway and/or breathing and/or circulation problems.

The lack of any consistent clinical manifestation and a range of possible presentations cause diagnostic difficulty

There is a range of signs and symptoms, none of which are entirely specific for an anaphylactic reaction; however, certain combinations of signs make the diagnosis of an anaphylactic reaction more likely.

When recognising and treating any acutely ill patient, a rational ABCDE approach must be followed and life-threatening problems treated as they are recognised

Anaphylaxis is likely when all of the following 3 criteria are met:
- Sudden onset and rapid progression of symptoms
- Life-threatening Airway and/or Breathing and/or Circulation problems
- Skin and/or mucosal changes (flushing, urticaria, angioedema)

The following supports the diagnosis:
- Exposure to a known allergen for the patient

Remember:
- Skin or mucosal changes alone are not a sign of an anaphylactic reaction
- Skin and mucosal changes can be subtle or absent in up to 20% of reactions (some patients can have only a decrease in blood pressure, i.e., a Circulation problem)
- There can also be gastrointestinal symptoms (e.g. vomiting, abdominal pain, incontinence)

Sudden onset and rapid progression of symptoms
- The patient will feel and look unwell.
- Most reactions occur over several minutes. Rarely, reactions may be slower in onset.
- The time of onset of an anaphylactic reaction depends on the type of trigger.
- The patient is usually anxious and can experience a “sense of impending doom”.

Life-threatening Airway and/or Breathing and/or Circulation problems
Patients can have either an A or B or C problem or any combination. Use the ABCDE approach to recognise these.

Airway problems:
- Airway swelling, e.g., throat and tongue swelling (pharyngeal/laryngeal oedema).
- The patient has difficulty in breathing and swallowing and feels that the throat is closing up.
- Hoarse voice.
- Stridor – this is a high-pitched inspiratory noise caused by upper airway obstruction.

Breathing problems:
- Shortness of breath – increased respiratory rate.
- Wheeze.
- Patient becoming tired.
- Confusion caused by hypoxia.
- Cyanosis (appears blue) – this is usually a late sign.
- Respiratory arrest.

Circulation problems:
- Signs of shock – pale, clammy.
- Increased pulse rate (tachycardia).

- Low blood pressure (hypotension) – feeling faint (dizziness), collapse.
- Decreased conscious level or loss of consciousness
- Anaphylaxis can cause myocardial ischemia and electrocardiograph (ECG) changes even in individuals with normal coronary arteries.
- Cardiac arrest.

Circulation problems (often referred to as anaphylactic shock) can be caused by direct myocardial depression, vasodilation and capillary leak, and loss of fluid from the circulation.
Bradycardia (a slow pulse) is usually a late feature, often preceding cardiac arrest. The circulatory effects do not respond, or respond only transiently, to simple measures such as lying the patient down and raising the legs.

Patients with anaphylaxis can deteriorate if made to sit up or stand up.

The above Airway, Breathing and Circulation problems can all alter the patient's neurological status (Disability problems) because of decreased brain perfusion.

There may be confusion, agitation and loss of consciousness.
Patients can also have gastro-intestinal symptoms (abdominal pain, incontinence, vomiting).

Skin and/or mucosal changes

- These should be assessed as part of the Exposure when using the ABCDE approach. They are often the first feature and present in over 80% of anaphylactic reactions. They can be subtle or dramatic.
- There may be just skin, just mucosal, or both skin and mucosal changes.
- There may be erythema – a patchy, or generalized, red rash.
- There may be urticaria (also called hives, nettle rash, weal's or welts), which can appear anywhere on the body. The weal's may be pale, pink or red, and may look like nettle stings. They can be different shapes and sizes, and are often surrounded by a red flare. They are usually itchy.
- Angioedema is similar to urticaria but involves swelling of deeper tissues, most commonly in the eyelids and lips, and sometimes in the mouth and throat.

Although skin changes can be worrying or distressing for patients and those treating them, skin changes without life-threatening airway, breathing or circulation problems do not signify an anaphylactic reaction. Reassuringly, most patients who have skin changes caused by allergy do not go on to develop an anaphylactic reaction. (www.acaai.org)

2.4 Management and Treatment

Coloured boxes taken from:
The Resuscitation Council Guidelines 2008

Management Algorithm

Patient feels unwell. Assess for signs of Anaphylaxis.
Stop administration of Systemic Anti-Cancer Drug.
Administer oxygen (10-15 litre/min) via facemask.

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Call for medical & nursing assistance.
Assess A.B.C.D.E

↓

IS AIRWAY COMPROMISED?

Airway NOT compromised

↓

Re-assess
BP >90 mm/Hg

↓

Was this a true anaphylactic reaction?

NO

↓

Recommence treatment under observation **following senior medical advice,**

And initially at a slower rate if appropriate.

YES

↓

Mild

No compromise to airway

Diagnosis – look for:

- Acute onset of illness
- Life-threatening **A**irway and/or **B**reathing and/or **C**irculation 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
- Hydrocortisone

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

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

- Adult: 500 micrograms IM (0.5ml)
- Child more than 12yrs: 500 micrograms IM (0.5ml)
- Child 6-12yrs: 300 micrograms IM (0.3ml)
- Child less than 6yrs: 150 micrograms IM (0.15ml)

Adrenaline IV to be given **only by experienced specialists**

3. IV fluid challenge:
Adult – 500-1000ml
Child – crystalloid 20ml/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	10mg	200mg
Child 6 – 12 years	5mg	100mg
Child 6 months to 6 years	2.5mg	50mg
Child less than 6 months	250 micrograms/kg	25mg

Nursing Management

Scope:
All nursing staff responsible for the administration of systemic anti-cancer therapy.

Objective:
To ensure prompt and efficient action is taken in the event of anaphylaxis to minimise the effects for the patient.
To act in such a manner as to maintain the well-being of the patient.

Responsibilities:
It is the responsibility of the individual trained nurse, skilled in administration of systemic anti-cancer therapy to recognise when anaphylaxis has occurred and what action is required to minimise effects.

Documentation:
- The Code: Professional Standards of Practice and Behavior for Nurses and Midwives (NMC 2015)
- Standards for Medicines Management (NMC 2007)
- UK Resuscitation Council Guidelines – Adult Anaphylactic Reactions (2008)
- The Administration of Cytotoxic Chemotherapy (RCN 1998)
- Local Trust nursing documentation
- Local Trust Incident Reporting System (DATIX)
- Suspected Adverse Drug Reaction Form (BNF most recent edition)
- Chemotherapy Prescription Chart/Journal on ARIA
- Associated Trust protocols/guidelines

Procedure:
Prior to the administration of systemic anti-cancer therapy the nurse must be familiar with the likelihood of the drug causing anaphylaxis or reaction, mechanisms of anaphylaxis, and be familiar with local emergency equipment and procedures.
Provide the patient with appropriate information to enable them to identify signs of treatment-induced anaphylaxis and emphasise the need to report these signs immediately if they occur.
Ascertain if any pre-treatment steroids have been taken; or are to be administered prior to chemotherapy.

At first signs of reaction:
- Cease administration of systemic anti-cancer therapy. Summon medical and nursing assistance.
- Recline the patient to a comfortable position, legs elevated if possible.
- Administer oxygen at high flow rates (10 – 15 litres/min) via facemask.
- Rapidly evaluate vital signs (pulse, BP, respirations, skin changes – 'ABC').

If there is no increase in severity of reaction, particularly no compromise to airway or patient recovers; systemic anti-cancer therapy administration may be recommenced under continued supervision and dependent on senior Haematology or Oncology advice.

OR If reaction becomes more severe:
- Call for immediate emergency assistance and equipment (Local Trust crash team). Do not give any more systemic anti-cancer therapy.
- Monitor patient airway.
- Prepare for administration of appropriate drugs (as per Resuscitation Council Guidelines and local Trust guidelines).

Adrenaline (Epinephrine) should be administered IM to all patients with any signs of compromise to airway (Resuscitation Council Guidelines 2008)
(Adrenaline may be repeated 5 minutes after initial dose).
Adrenaline to be administered in accordance with local Trust guidelines (following Resuscitation Council guidelines 2008 and most recent edition of British National Formulary).

If cardiac arrest procedure not required: Continue treatment for anaphylactic reaction as per Resuscitation Council Guidelines and local Trust guidelines.

Other concurrent measures:

- Prescribed antihistamine to be administered.
- Administer 1 – 2 litres of fluid (crystalloid preferred) via rapid free flow infusion.
- Prescribed bronchodilator to be administered.
- Prescribed corticosteroid to be administered (at discretion of senior Haematology / Oncology advice and dependent on whether other steroid therapy has been given pre-treatment).
- Provide psychological support to the patient and their family. Reassure and explain to the patient and any relatives what is being done and what should be expected to happen.
- Comfort may be promoted and distress reduced with the administration of prescribed analgesics and anti-emetics. Evaluate their effectiveness following administration.
- Ensure the episode is accurately documented (to include sensitivity) in appropriate local nursing, medical and electronic records.
- Follow local Trust guidelines for reporting of incident.
- Patient to be admitted to ward at discretion of senior Haematology / Oncology advice (if not already an 'in patient')

2.5 Documentation

Complete Intervention Report Form for the Management of Systemic Anti-Cancer Reactions in Adults (See appendix 1) and file in patients' medical/nursing notes.

3 PROCESS FOR MONITORING COMPLIANCE

Qualified staff new to the service will be expected to attend the 3 day Chemotherapy Competency Induction Workshop to be entered into the work based learning Chemotherapy Competency Programme (NEYHCA 2013). The monitoring of compliance with and clinical competency of staff regarding the Management of Systemic Anti-cancer Therapy Reactions in Adults will be undertaken by the ward/department managers with support from the Chemotherapy Nurse Specialist Team. All nursing staff will complete required competency and will reviewed yearly, with specific regard to health and safety (Topic 5) and Oncological Emergencies (Topic 6) Chemotherapy Competency Programme.

All staff must attend required HEY Trust yearly updates as part of the resuscitation guidance.

All staff should complete HEY247 elearning course – Emergency Treatment of Anaphylactic Reactions

Guidelines will be monitored and reviewed as per the cancer standards and Peer Review process with advice and support from the Trust Chemotherapy Committee Meeting (CCM) members.

All incidents relating to systemic anti-cancer reactions must be documented accordingly as per guidelines and reported via HEY Trust DATIX system and reviewed by the CCM.

4 REFERENCES

www.acaai.org

Allwood M & Wright P eds. (2002) The Cytotoxics Handbook
4th Edition Rawcliffe Medical Press Ltd.

BNF Most recent edition.

Castells et al (2008) Hypersensitivity Reactions to Chemotherapy: Outcomes and safety of rapid desensitization in 413 cases.
Journal of Allergy and Clinical Immunology. 122:574-80.

Dougherty L & Lamb J (2008) Intravenous Therapy In Nursing Practice. 2nd Edition
Blackwell Publishing Ltd

Ferns T & Chojnacka I (2003) The causes of anaphylaxis and its management in adults.
British Journal of Nursing September 25 – October 8 2003. 12:17:1006-1014

Jurewicz MA (2000) Anaphylaxis: when the body overreacts.
Nursing 2000 30:7:58-61.

Kelso J.M. (2004) The rate of systemic reactions to immunotherapy injections is the same whether or not the dose is reduced after local reaction.
Annals of Allergy Asthma & Immunology. Feb 2004. 92:2:225-228

Lieberman P (2005) Biphasic anaphylactic reactions.
Annals of Allergy, Asthma and Immunology. 95:3 217-226

Mistovich J (2008) Anaphylactic and Anaphylactoid Reactions
www.EMS1.com

Moor J & Jennison N (2003) Standardisation of anaphylaxis management in an acute hospital trust – a model for change.
Nursing Times 100:15:32-34.

NMC (2015) The Code: Professional standards of practice and behavior for nurses and midwives

Nursing Centre (2000) Emergency: Chemotherapy- Induced Hypersensitivity Reactions.
American Journal of Nursing. April 2000. 100:4:53

Page C, Curtis M, Sutter M, Walker M & Hoffman B (2002) Integrated Pharmacology.
2nd Edition. Mosby International Ltd

Resuscitation Council UK (2008). Annotated July 2012 with links to NICE guidance

Document Control			
Reference No:		**First published:**	June 2002
Version:	3.0	**Current Version Published:**	February 2017
Lead Director:	Russell Patmore	**Review Date:**	August 2020
Document Managed by Name:	Chemotherapy Nurse Specialist Team	**Ratification Committee:**	
Document Managed by Title:	Chemotherapy Nurse Specialist Team	**Date EIA Completed:**	

Consultation Process

Chemotherapy Nurse Specialist Team
Chemotherapy Committee Meeting Members
Russell Patmore *Lead Director*
Dr Roy *Clinical Lead*
Dr Dhadda *Head of Clinical Chemotherapy Services*
Mandi Elliott *CNS of Clinical Chemotherapy Services*
Clinical Effectiveness Group
Policies & Practice Group

Key words (to aid intranet searching)

Management of Systemic Anti-Cancer Reactions in Adults

Target Audience

All staff	Clinical Staff Only	Non-Clinical Staff Only
Managers	Nursing Staff Only	Medical Staff Only

Version Control

Date	Version	Author	Revision description
February 2017	3.0	Chemotherapy Nurse Specialist Team	Adapted from NEYHCA with change of title, minor rewording throughout and update of references.

http://intranet/resus/pdf/reaction.pdf

Appendix 1

Intervention Report Form for the Management of Systemic Anti-Cancer Therapy Reactions in Adults

Date:	Ward/OPD	
Patients name: (Patient sticker)		
HEY/NHS No	DOB	Consultant

Diagnosis: ……
Regimen: …… Cycle No.: ……
IV Access: ……
Drugs Involved: ……
……
Amount of drug administered ~ prior to onset of reaction (mls)

Other drugs given concurrently (state if oral or IV.) ~ To include prophylactic medication, i.e.: anti-emetics:
……
……

Brief account of symptoms experienced by patient:

Medical staff notified and present:

Drugs administered:

Nursing Action:

Follow up measures: (to include investigations, ie: blood samples)

Suspected Adverse Drug Reaction Form (BNF)

Documentation completed: Medical Notes: ☐ Nursing Records: ☐ ARIA: ☐ Datix: ☐

Print Name & Designation: ……

Signed: ……