

RADIOLOGY DIRECTORATE

RADIOLOGY GUIDELINES FOR THE USE OF IODINATED CONTRAST MEDIA IN ADULTS

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

INTRODUCTION

Use of iodinated contrast has increased exponentially in recent years and although relatively safe there are subgroups of patients for whom the administration of iodinated contrast media poses increased risk. Patients covered by this guideline are those for whom there is a likelihood of intravascular administration of iodinated contrast during their investigations.

This guideline is derived from the RANZCR 2016 and 2018 published guidelines adopted by the Royal College of Radiologists since 2017, and takes into account the UK NICE recommendations on Acute kidney injury 2019 (NG148).

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS: All clinicians and staff groups able to request or deliver contrast enhanced examinations.

Lead Clinician(s)

Dr Sarah Parsonage	Consultant Radiologist and CT Lead
Dr Martin Ferring	Consultant Renal Physician
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Key amendments to this guideline

Date	Amendment	Approved by:
14 th December 2022	Update on use of EGFR for renal function marker for all patients Updated pre hydration protocols	Radiology directorate

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including approval and review dates.



RADIOLOGY GUIDELINES FOR THE USE OF IODINATED CONTRAST MEDIA IN ADULTS

Introduction

lodinated contrast (i.e. Radiation absorbent material used systemically to assist in the differentiation of physiological and pathological processes) is employed in a number of radiological modalities, mainly CT, arteriography and venography.

Intravascular contrast media has been available for approximately a century. The first description of renal toxicity associated with contrast media was published in 1954 by Bartels and colleagues¹. Since then, in line with the increasing use of contrast agents, particularly in the 1970's there have been thousands of reports of contrast induced renal dysfunction, anaphylactic and idiosyncratic reactions. Developments in contrast agents have subsequently resulted in a marked decrease in the number of general adverse events. Approximately 1% of patients are thought to have minor reactions to intravascular iodinated contrast with less than 1 in 100,000 experiencing a severe reaction. The rate of contrast induced nephropathy remains controversial however there has been a substantial amount of new evidence since the previous trust guidance which has resulted in revisions to international guidance including the American College of Radiology Manual on Contrast Media V10, 2015, European Society of Uroradiology and the RANZCR guidelines² which have more recently been adopted by the Roval College of Radiologists and around which this guidance is derived. To summarise, the more recent studies have raised questions about whether intravenous administration of iodinated contrast media results in a clinically significant rate of biochemical evidence of renal function impairment.

All modern contrast agents have similar pharmacokinetic properties with low lipid solubility, low chemical activity with body fluids and small molecular weights. Excretion half-life in patients with normal renal function is 1-2 hours with 99% excreted via the kidneys and 1% via the intestine.

Modern radiographic-contrast materials are largely non-ionic. These agents are more biologically inert and subsequently are better tolerated with decreased toxicity when compared to previous generation ionic agents. These are of variable osmolality with higher osmolality agents being more associated with adverse reactions such as pain, vasodilatation, hypotension, thrombosis and arterial spasm.

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Hypersensitivity Reaction to Iodinated Contrast Media

Hypersensitivity reactions to iodinated contrast media are classified into immediate and delayed reactions. Reactions are further classified as mild, moderate or severe.

Mild contrast media reactions include flushing, nausea, pruritus, vomiting, headache and mild urticaria. These are usually self-limiting and resolve without specific treatment and may be seen in up to 1% of patients after non-ionic low osmolality contrast media administration.

Moderate contrast media reactions include severe vomiting, marked urticarial, bronchospasm or other respiratory symptoms, facial/laryngeal oedema and vasovagal attacks.

Severe contrast media reactions include hypovolaemic shock, respiratory arrest, cardiac arrest and convulsions. Severe anaphylactic reactions are uncommon, occurring in less than 1 in 100,000 patients.

Delayed hypersensitivity reactions to contrast media occur between one hour and one week following administration of contrast media. These are typically skin reactions with maculopapular rash being most common. Less frequent reactions include urticarial, angioedema and erythema. Delayed hypersensitivity reactions are not typically associated with laryngeal oedema or bronchospasm. The reported incidence of delayed type hypersensitivity reaction is 4% or less.

- In order to minimise the risk of iodinated contrast media reaction the department should have a system in place to identify individuals at increased risk of adverse reaction. Information which should be obtained from the patient, responsible adult or referring physician before iodinated contrast media administration include:
 - History and nature of a previous reaction to iodinated contrast media or history of a reaction requiring medical treatment (Tenfold increased risk with estimated likelihood of reaction between 8-60%).
 - History of asthma (Six fold increased risk, higher in patients whose asthma is poorly controlled)
 - Previous significant allergic reactions to other substances or history of eczema (Three to five fold increased risk, although most reactions are mild)
 - Current use of beta blockers (No increased risk, however reaction is more likely to be moderate to severe)
- There is no increased risk associated specifically with shellfish allergy, nor from topical iodine allergy.

For patients who are at increased risk of contrast media reaction:

- Consider performing a non-contrast media study or use alternative imaging modalities which do not require iodinated contrast.
- If after considering the risks and benefits of the procedure it is decided to proceed with a contrast media enhanced study:

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- If possible, use a different non-ionic or iso-osmolar contrast media to that which caused a reaction.
- Maintain close medical supervision.
- Leave the cannula in place and keep the patient under observation for 30 minutes after contrast media administration.
- Ensure emergency drugs, equipment and appropriately trained staff are immediately available.
- Be prepared to treat any reaction promptly.
- Consider the use of premedication (see below).

Premedication of patients with prior reaction to iodinated contrast media

Premedication with corticosteroids, with or without antihistamines has been shown to reduce the likelihood and severity of anaphylactic reactions but there is no evidence that it reduces the likelihood of death resulting from breakthrough anaphylactic reaction.

If required, the premedication regime below should be used:

- Prednisolone 50mg orally 13 hours and 1 hour before contrast media administration.
- Oral non-sedating antihistamines may be added to the above premedication.

Contrast Media Induced Kidney Injury and Metformin Associated Lactic Acidosis

Definition

Contrast-medium-induced nephropathy (CIN) is defined as an acute kidney injury caused by exposure to intravascular iodinated contrast media, resulting in a decrease in GFR³. The decline in GFR caused by CIN is usually documented by an increase in serum creatinine relative to baseline levels that usually occurs within 72 hours of exposure to iodinated contrast media, with a return to baseline or near baseline within 7 to 10 days in most cases⁴. However, in some instances this proceeds to acute renal failure requiring temporary dialysis support. It is not possible to predict exactly which patients will progress to renal failure, but the risk rises the greater the pre-procedural renal impairment.

Pathogenesis

Contrast media is thought to cause renal toxicity via the following mechanisms:

- 1: Renal cortical arteriolar constriction (endothelin)
- 2: Renal tubular toxicity via the release of free radicals

At risk patients are those whose nephrons are exposed to the direct toxic effects of contrast for longer. These include those with decreased GFR (greater contrast load per functioning nephron), decreased renal perfusion e.g. congestive cardiac failure, hypotension or volume depletion (increases exposure duration of nephron to contrast), and impaired endothelial

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response mechanisms e.g. diabetics, those taking diuretics or NSAIDS. Diabetes also impairs the ability of the nephron to produce nitric oxide which further compromises renal perfusion. Intra-arterial contrast may result in a higher contrast load and thus higher risk for CIN than if contrast is given intravenously.

Risk identification and stratification

Prior to intravascular administration of iodinated contrast media patients should be asked the following questions. If present, an eGFR should be obtained prior to iodinated contrast media administration in non-emergency patients:

- Known kidney disease (in particular, eGFR < 30, or presence of acute kidney injury alert, or renal transplant)
- Presence of diabetes
- Current use of a drug containing Metformin

Non-anuric patients currently on short or long term dialysis may benefit consultation with a renal physician prior to iodinated contrast media administration to schedule their dialysis shortly after the contrast scan.

Acutely ill patients are often at risk of acute kidney injury (AKI). AKI is defined by a significant rise in Creatinine above baseline (ie a rise by 50%, or an increase by 26 mcmol/L or more within 24h), or reduced urine output (not always available). In AKI, the Creatinine rise has some delay; looking out for the AKI alert for acute kidney injury produced by the biochemistry lab may help identify AKI particularly in patients with near-normal Creatinine values. In patients with chronic kidney disease (CKD) and stable kidney function, **eGFR** is less reliable in patients with reduced muscle mass (eg cachexia or post limb amputation) and will tend to overestimate renal function in these groups: consider these patients for pre/post hydration even with apparently preserved renal function. Also, patients with CKD are very prone to AKI in the context of any acute illness, surgery or hospital admission.

Age should not be considered an independent risk factor.

The current literature suggests no measurable risk in patient with eGFR >45 ml/min/1.73m². There is uncertain risk associated with eGFR 30-45 ml/min/1.73m². The area of greatest controversy is in those patients with eGFR <30ml/min/1.73m² with the odds of CIN occurring in this group as a result of a single intravenous dose of iodinated contrast media being either the same as or up to 7 times greater than patients with normal renal function. Baseline renal function remains the most significant predictor of contrast induced nephropathy. Actively deteriorating renal function is an independent risk factor for contrast induced nephropathy.

The AusDiab study established that the frequency of undiagnosed severe (eGFR less than 30ml/min/1.73m²) renal function impairment in Australian adults aged over 25 years was less than 1%.

Risk reduction

In patients with severe renal function impairment (eGFR less than 30ml/min/1.73m²) or actively deteriorating renal function (acute kidney injury) careful weighing of the risk versus benefit of iodinated contrast media administration needs to be undertaken. Consideration should be given to peri-procedural renal protection using intravenous hydration with 0.9% sodium chloride. However, severe renal function impairment should not be regarded as an absolute contraindication to medically indicated iodinated contrast media administration. The

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NICE guidance on AKI concluded that for outpatients, oral pre- and post-hydration was not inferior to IV hydration; for most outpatients, oral hydration may be adequate.

There remains no proven added benefit to use the use of N-Acetylcysteine or Sodium bicarbonate.

Guideline - Intravenous contrast

Intravascular iodinated contrast media should be given to any patient regardless of renal function status if the perceived diagnostic benefit to the patient, in the opinion of the radiologist and the referrer, justifies the administration.

Emergency imaging procedures requiring contrast media administration e.g. acute stroke, acute bleeding, trauma etc. should not be delayed in order to obtain renal function testing results prior to the procedure.

Inpatients:

Emergency imaging: If imaging is vital for an immediately life threatening condition (risk of delaying scan worse than risk of contrast nephropathy), then imaging should not be delayed. Patients with any identified risk factors for renal impairment (see below) should receive preventive measures empirically. This should consist of a pre-procedural fluid challenge (250-500ml 0.9% sodium chloride or adequate amount required to correct hypovolaemia and normalise blood pressure / urine output) and post procedure intravenous sodium chloride of at least 1ml/kg/hr for 4 hours if these measures are deemed safe for the patient.

Patients with acute renal dysfunction may benefit from postponement of non-urgent Imaging, if appropriate, to allow optimisation of renal function.

Please check for renal risk, ie:

biochemistry results show eGFR <30, or an acute kidney injury (AKI) alert as 1, 2, 3; or if the patient has a renal transplant.

- 1. **Check renal function** in all patients before (within 3 days) a procedure potentially requiring a contrast study or when an imaging modality is being contemplated in which contrast is frequently administered e.g. CT.
- 2. Check if eGFR < 30 or acute kidney injury alert AKI 1,2 or 3 present on biochemistry report
- If eGFR < 30 ml/min/1.73m2, or AKI alert present or kidney transplant: If imaging can wait, consider an alternative modality e.g. US/S, MR or NECT or wait until renal function is improved. If renal function cannot be improved, or delay of imaging is inappropriate, please follow the steps below:
 - a. **Pre- and post-hydrate** with IV 0.9% sodium chloride all inpatients with eGFR <30 ml/min/1.73m2 or AKI alert 1,2 or 3 at a rate of 1.5ml/kg/hr for at least 2 hours immediately before scan and 4 hours after scan (to be arranged by referrer). Note exceptions below (*)

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- b. **Nephrotoxic medication** (to be arranged by referrer) e.g. NSAIDS should ideally be stopped 24 hours prior to the investigation and for 3 days after. Ideally, Gentamicin should be avoided please discuss with duty microbiologist. See also Metformin guidance below (pause for 48h post contrast injection).
- c. Advise recheck of renal function daily for 3 days following iodinated contrast administration (to be arranged by referrer).
- d. Advise fluid balance chart for 3 days post iodinated contrast administration (to be arranged by referrer).

(*) EXCEPTIONS:

- In patients with clinical signs of significant fluid overload or pulmonary oedema, IV sodium chloridehydration is contra-indicated. Consider pausing diuretics and ACE-inhibitors / angiotensin blockers for 24 hours on day of contrast. In patients with known cardiac dysfunction but no signs of fluid overload, hydration should occur at a slower rate 0.5ml/kg/hr with frequent monitoring of their clinical hydration status, so as to avoid over hydration.
- The slower rate of 0.5ml/kg/hr also applies in Paediatric patients.
- Anuric Dialysis dependant patients do not require preventative measures, oliguric dialysis patients benefit from early post procedure dialysis and so discussion with a nephrologist is advised

Outpatients/GP referrals:

- 1. Prior to referral patients should be asked the following.
 - a. Known kidney disease (including renal transplant)
 - b. Presence of diabetes
 - c. Current use of a drug containing Metformin

Non-anuric patients currently on short or long term dialysis may require consultation with a renal physician prior to iodinated contrast media administration to schedule their dialysis soon after the contrast scan.

If any of the above are present, an eGFR should be provided (within 3 months of anticipated study) or requested at the time of imaging request.

- 2. Outpatients or GP referrals with eGFR (greater than or equal to)>30: No precautions are required. (Please note that the eGFR may be overestimated in patients with reduced muscle mass (eg cachexia or post limb amputation); in such patients please consider guidance for eGFR < 30 below).
- 3. **Outpatients with eGFR <30:** Consider alternative imaging modality e.g. NECT, USS or MRI. If contrast is required then:

a. Hydration: The patient should be asked to drink 500ml water (alternatively squash/ tea) before and 500ml after the scan. -Consider seeking specialist

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advice if eGFR < 15 (eg renal A&G), or if there is severe hyponatraemia Na < 125 mmol/L (eg endocrine A&G): to be arranged by the referrer.

- b. **Nephrotoxic medication** e.g. NSAIDS should be stopped 24 hours prior to the investigation (to be arranged by referrer). See also Metformin guidance below.
- c. **Pause diuretics** on day of scan unless advised differently by speciality consultant (to be arranged by referrer).
- d. Advise ideally to recheck blood test (renal function and eGFR) within 72 hours of iodinated contrast administration (to be arranged by referrer)
- e. **If patient acutely unwell on day of scan** (eg Diarrhoea and vomiting), patient to be advised not to attend and seek medical help. Scan to be rebooked for when patient recovered

General Exclusions: In the instance of requiring a post contrast examination of the head following an abnormal unenhanced CT and in the absence of known renal impairment this should proceed, as clinical delay is likely to be of greater harm than the low dose of contrast utilised for this study.

Guideline – Intra-arterial contrast:

- 1. Check Urea and Electrolytes within 3 days for inpatients, within 4 weeks for outpatients/elective procedures
- 2. If eGFR >45 no precautions are required.
- 3. If eGFR <45 or AKI alert 1,2 or 3 then the peri-procedural hydration protocol should be followed with 2ml/kg/hr for 3 hours pre-procedure and 1ml/kg/hr for 6 hours post procedure. Contrast load should be minimised. In patients with poor cardiac function and/ or taking significant quantities of diuretics and in whom IV fluids may be dangerous, withholding the diuretics in the 24 hrs pre-procedure alone may be sufficient. Please consider referral to nephrologist for advice.

It is advised that patients with low eGFR should have their eGFR and creatinine re-assessed 24-72 hours post examination.

Metformin

- Intravenous administration of iodinated contrast media:
 - Patients receiving intravenous iodinated contrast media with eGFR above 30mL/min/1.73m2 should continue taking metformin
 - Patients with an unknown recent eGFR or an eGFR less than 30mL/min/1.73m2, or who are unwell or have deteriorating renal function should cease metformin for at least 48 hours from the time of the examination and an eGFR performed prior to restarting Metformin.
- Intra-arterial administration of iodinated contrast media:

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- Patients undergoing an intra-arterial procedure requiring iodinated contrast media with an eGFR above 45 ml/min/1.73m2 should continue taking metformin.
- Patients undergoing an intra-arterial procedure involving larger volumes of contrast media and/or a procedure involving a risk of renal embolization with an unknown recent eGFR or eGFR of less than 45 ml/min/1.73m2, or who are unwell or have deteriorating renal function should cease metformin for at least 48 hours following the intra-arterial administration of contrast media and have eGFR estimated prior to restarting metformin.

Other medical conditions that need consideration prior to administration of lodinated Contrast Media

Thyroid Disease

Patients with untreated hyperthyroidism or hyperfunctioning thyroid nodule with or without a multinodular goitre are at increased risk of developing clinically important thyrotoxicosis following administration of iodinated contrast media. However, a recent study has suggested that the biochemical evidence of both hyper and hypothyroidism seen following administration of iodinated contrast media is both temporary and subclinical.

The large amount of iodine within contrast media can however prevent uptake of thyroid specific radio-isotopes for up to 8 weeks after contrast media administration.

- Patients with known or suspected hyperthyroidism should be investigated and treated prior to contrast media administration.
- If contrast media administration is urgently required in a patient with known, untreated hyperthyroidism, the advice of an endocrinologist should be sought whenever possible prior to administration of iodinated contrast.
- Patients with untreated hyperthyroidism who receive iodinated contrast media should be informed of the possibility of developing hyperthyroidism over the coming weeks.
- Patients who are known to have a hyperfunctioning thyroid nodule, with or without associated multinodular goitre, are at increased risk of thyrotoxicosis following intravenous iodinated contrast media administration, even if they have no clinical / biochemical evidence of hyperthyroidism. Patients in this situation should be advised about this risk and monitored for the development of this complication in the weeks following the injection.

Myasthenia Gravis

It remains controversial whether iodinated contrast media are contra-indicated in this group however there is evidence that symptoms of myasthenia, including difficulty breathing, may be worsened following administration of iodinated contrast media. Patients should be advised of the possibility of worsened symptoms prior to administration.

Interleukin-2 (IL-2) therapy

Patients currently taking or who have finished IL-2 therapy in the past 6 months should be cautioned regarding a possible mild increase in the risk of delayed hypersensitivity contrast media reaction. No further precautions are required.

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Breast Feeding

Cessation of breast feeding or expression and discarding of breast milk after iodinated contrast media administration are not required.

Pregnancy

Limited cases of pregnant women receiving intravenous iodinated contrast media during pregnancy have shown no significant increase in the frequency of malformations or adverse effects. Animal studies have not shown evidence of an increased occurrence of foetal injury. A recent study has shown an increased risk of perinatal biochemical hypothyroidism following administration of iodinated contrast media for hystero-salpingogram. It is unclear whether this risk applies to intravenous water soluble contrast media.

• Infants born to women who have received iodinated contrast media while pregnant should have testing for hypothyroidism in the neonatal period. This is routinely performed in the UK.

PAEDIATRIC ADMINISTRATION OF IODINATED CONTRAST MEDIA –SPECIAL CONSIDERATIONS

The information contained in the section on Anaphylactic Reaction applies equally to children

ORAL AND OTHER NON-INTRAVASCULAR CONTRAST MEDIA ADMINISTRATION

Small amounts of iodinated contrast media are absorbed from the gastrointestinal tract after oral administration. It is estimated that up to 1% of the administered dose is absorbed in healthy individuals, and potentially more in people with inflammation in the gastrointestinal tract. While anaphylactic reactions resulting from non-vascular administration of iodinated contrast media are rare, the same precautions should be taken as with intravascular administration. Side effects due to the physical properties of oral iodinated contrast media are common. Pulmonary oedema due to the aspiration of ionic contrast media into the lungs can be life threatening. Common gastrointestinal side effects include diarrhoea, nausea and vomiting. These are usually self-limiting, but can result in serious electrolyte disturbances in seriously ill or dehydrated patients.

- Anaphylactic reactions can occur with non-vascular administration of iodinated contrast media and the same precautions should be taken as with intravascular use.
- Severe electrolyte disturbances and or dehydration should be corrected where
 possible prior to the administration of oral iodinated contrast media and electrolytes
 should be monitored in severely ill patients or those with severe diarrhoea and/or
 vomiting.
- Ionic contrast media should not be given orally to patients at risk of aspiration. Nonionic contrast media or barium sulphate can be used as safer alternatives.

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MANAGEMENT OF ANAPHYLACTIC IODINATED CONTRASTMEDIA REACTION

Severity	Signs/Symptoms	Treatment
Mild	MildNausea/Vomiting	Supportive measures(antiemetics if prolonged vomiting)
	Urticaria	Supportive measures
	Urticaria(protracted)	
		Non-sedating antihistamine(s)
Moderate	Urticaria	Non-sedating antihistamine(s)
		Consider use of adrenaline1:1000 •In adults:0.1-0.25ml(0.1-0.25mg) intramuscularly into the anterolateral thigh–repeat as necessary •Inchildren:0.01mg/kg intramuscularly upto 0.3mg maximum dose
	Bronchospasm or	Keep supine; allow patient to sit if dyspnoeic
	other respiratory symptoms	Oxygen by mask(6-10L/min). Salbutamol or Terbutaline metered dose inhaler(2-3 deep inhalations)
		In more severe cases give Salbutamol or adrenalin by nebuliser.
		 Consider adrenaline Normal blood pressure In adults: 1:1,000, 0.1-0.5ml(0.1-0.5mg) intra-muscularly (use smaller dose in patients with coronary artery disease or elderly patients) In paediatric patients: 0.01mg/kg upto 0.3mg intramuscularly Decreased blood pressure In adults: 1:1,000,0.5ml(0.5mg) intramuscularly In paediatric patients:0.01mg/kg intramuscularly
	Hypotension	Isolated hypotension •Keep supine; elevate patient's legs •Oxygen by mask (6-10L/min) •Intravenous fluid : rapidly, 0.9 % sodium chloride or lactated Ringer's solution •If unresponsive:adrenaline:1:1,000, 0.5ml(0.5mg) intramuscularly, repeat as needed Vaso-vagal reaction (hypotension and bradycardia) •Keep supine elevate patient's logs
		 Keep supine,elevate patient's legs Oxygen by mask(6-10L/min) Atropine In adults 0.6-1.0mg intravenously, repeat if necessary after 3-5min, to 3mg total (0.04mg/kg). In paediatric patients give 0.02mg/kg intravenously (max.0.6mg per dose) repeat if necessary to 2mg total.

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		 Intravenous fluids: rapid infusion of 0.9 % sodium chloride or Hartmann's solution 20ml/kg, repeat as necessary.
Severe	Respiratory or	Call for resuscitation team
	circulatory collapse and/or seizures	Keep supine. Allow patient to sit if dyspnoeic.
		Suction and maintain airway as needed
		Oxygen by mask(6-10L/min), ventilate patient if required
		Intramuscular adrenaline into the anterolateral thigh
		•In adults (and in children greater than 25kgs), adrenaline1:1000
		less than 50kg give 0.25-0.5mL
		greater than 50kg give 0.5mL
		•In children, Adrenaline1:1,000
		1year 10kg give 0.1mL
		3years 15kg give 0.15mL
		5years 20kg give0.2mL
		8years 25kg give0.25mL
	•If necessary, repeat intramuscular dose every 5 minutes.	
		•Large doses of adrenaline maybe needed, upto a maximum of 5mL(5mg).
		•In adrenaline resistant cases, especially if the patient has taken
		beta blocking drugs, consider glucagon1-2mg intravenous over 5
		minutes.
		•If the patient remains shocked after two intramuscular doses,
		consider an adrenaline infusion to restore blood pressure.
		Intravenous fluids (e.g. 0.9% sodium chloride or Hartmann's
		solution 20mL/kg); continue as necessary.
		Additional measures
		 Bronchodilators: for bronchospasm, give salbutamol or via
		nebuliser or aerosol with spacer device
		 Corticosteroids: Hydrocortisone 2-6mg/kg or Dexamethasone
		0.1-0.4mg/kg intravenously•
		Nebulised adrenaline: Maybe tried for laryngeal oedema
		(5mlof1:1000)
		Supportive measures
		•Observe vital signs frequently; monitor ECG and pulse oximetry
		•Arrange for transfer to hospital if reaction occurs in an outpatien
		facility
		•Keep under observation for at least 4-6 hours after complete
		resolution of signs and symptoms, as biphasic reactions may occur

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MONITORING TOOL

Annual audit will be performed on a series of consequential patient attendances at each site. To be carried out by the Radiology directorate

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CONTRIBUTION LIST

Key individuals involved in developing the document

Name	Designation
Dr Sarah Parsonage	Consultant Radiologist and CT Lead

Circulated to the following individuals for comments

Name	Designation
Radiologists Countywide	
Amy Ensell-Harper, Liz Llewellyn,	CT Superintendant Radiographers
Tina Bater	

Circulated to the following CD's/Heads of dept for comments from their directorates / departments

Name	Directorate / Department
Dr Inderjeet Nagra	CD Radiology
Dr Martin Ferring	Consultant Renal and General Medicine

Circulated to the chair of the following committee's / groups for comments

Name	Committee / group
	Radiology Directorate Governance group
	Medicines Safety Committee

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