Delayed Hypersensitivity Reactions

R1. In order to minimise the risk of iodinated contrast media administration, the medical imaging department should have systems in place to identify individuals at increased risk of adverse reactions to iodinated contrast media. A point of care tool to facilitate this is provided at the end of this document.

a) Although beta adrenergic blocking medications do not appear to significantly increase the incidence of an anaphylactic contrast media reaction, any such reaction is more likely to be moderate or severe. In addition, the effects of intramuscular adrenaline in patients taking beta blockers may be reduced and intravenous glucagon may be required in addition to adrenaline in this situation.

b) Information which should be obtained from the patient, carer and/or referring clinician before iodinated contrast media administration include:

i. History and nature of a previous reaction to iodinated contrast media or history of reaction requiring medical treatment

ii. History of asthma

iii. Previous significant allergic reactions to other substances or history of eczema

iv. Current use of beta adrenergic blockers

R2. In patients who are at increased risk of an anaphylactic reaction to iodinated contrast media:

a) Consider performing a non-contrast media study or use of alternative imaging modalities which do not require administration of iodinated contrast media (e.g. Ultrasound, MRI).

b) If, after considering the risks of a contrast media reaction and the potential benefits of the procedure, it is decided to proceed with the contrast media enhanced study:

i. Use a different non-ionic low or iso-osmolar contrast media to the one used previously in the setting of a prior reaction if possible

ii. Maintain close medical supervision

iii. Leave the cannula in place and keep the patient under observation for 30 minutes after contrast media administration

iv. Ensure emergency drugs and equipment for resuscitation are readily available

v. Be prepared to treat any adverse reaction promptly. Consider use of premedication (see below)
Premedication of Patients with Prior Anaphylactic Reactions to Iodinated Contrast Media

R3. 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 a breakthrough anaphylactic reaction.

a) If oral corticosteroid premedication is used, it must be commenced at least 6 hours prior to the contrast media study.

b) A typical premedication regimen for adults is:
   i. Prednisolone 50mg orally, given at 13 hours and 1 hour before contrast media administration.
   ii. Oral non-sedating antihistamines may be added to the above premedication regimen.

Contrast Media Induced Kidney Injury and Metformin Associated Lactic Acidosis

R4. 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 this administration.

R5. 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.

R6. The risk of intravenous contrast media related acute kidney injury (CI-AKI) is likely to be non-existent for patients with eGFR greater than 45 mL/min/1.73m2. No special precautions are recommended in this group prior to or following intravenous administration of iodinated contrast media.

R7. The risk is of intravenous CI-AKI is also very likely to be low or non-existent for patients with eGFR 30 - 45 mL/min/1.73m2. Universal use of periprocedural hydration in this group to prevent the theoretical risk of CI-AKI cannot be recommended but patients with impaired function in this range that is acutely deteriorating rather than stable may benefit from this intervention.

R8. In patients with severe renal function impairment (eGFR less than 30 ml/min/1.73m2) or actively deteriorating renal function (acute kidney injury) careful weighing of the risk versus the benefit of iodinated contrast media administration needs to be undertaken. Consideration should be given to periprocedural renal protection using intravenous hydration with 0.9% saline (see relevant section). However, severe renal function impairment should not be regarded as an absolute contraindication to medically indicated iodinated contrast media administration.

Clinical Estimation of Renal Function

R9. eGFR using the CKD-EPI formula using serum creatinine, patient age, gender and race, should be used in preference to serum creatinine to identify patients with severely impaired renal function.

R10. eGFR should not be relied upon as an accurate indicator of renal function in patients who are known to have acute kidney injury for any reason.
Screening Patients with Regard to Their Need for Renal Function Testing

R11. Prior to intravascular administration of iodinated contrast media patients should be asked the following. If present, an eGFR should be obtained prior to iodinated contrast media administration in non-emergency patients.

a) known kidney disease (including kidney transplant)

b) presence of diabetes

c) whether they are currently taking a drug containing metformin. (see Point of Care Risk Assessment of Patients Who Are To Receive Intravascular (Arterial Or Venous) Iodinated Contrast Media)

R12. Non-anuric patients currently on short or long term dialysis may require consultation with a renal physician prior to iodinated contrast media administration.

R13. Age should not be considered as an independent risk factor that should mandate testing as eGFR declines with age even in healthy individuals, due to the way it is calculated.

R14. The time elapsed between renal function testing and contrast media administration should be governed by clinical judgment based upon the likelihood that renal function has deteriorated to a clinically significant degree since the renal function was assessed.

Periprocedural Strategies to Mitigate the Risk of CI-AKI in Higher Risk Individuals

R15. For patients who are at higher risk of CI- AKI, pre and post procedural 0.9% IV saline is recommended as the first line preventive strategy to mitigate the risk of CI-AKI.

R16. The evidence in support of the additional benefit of N – acetyl cysteine and/or sodium bicarbonate alone or in combination with intravenous 0.9% saline is mixed and currently these additional measures are not recommended due to additional expense and complexity without clear evidence of incremental risk reduction.

Metformin and Contrast Media

R17. Intravenous administration of iodinated contrast media: Patients receiving intravenous iodinated contrast media with an eGFR above 30 ml/min/1.73 m2 should continue taking metformin. Patients with an unknown recent eGFR or an eGFR less than 30 ml/min/1.73 m2, or who are unwell or have deteriorating renal function should cease metformin for at least 48hrs from the time of the examination and an eGFR performed prior to restarting metformin.

R18. Intra-arterial administration of iodinated contrast media: Patients undergoing an intra-arterial procedure requiring iodinated contrast media with an eGFR above 45 ml/min/1.73 m2 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 embolisation with an unknown recent eGFR or an eGFR less than 45 ml/min/1.73 m2, or who are unwell or have deteriorating renal function should cease metformin for at least 48hrs following intra-arterial administration of contrast media and have eGFR estimated prior to restarting metformin.
Other Medical Conditions That Need to be Considered Before the Administration of Iodinated Contrast Media

Thyroid Disease

R19. Patients with known or suspected hyperthyroidism (clinical or biochemical) should be tested and treated for this in consultation with the referrer or an endocrinologist prior to contrast media administration. Treatment typically consists of beta blockade and carbimazole.

R20. If contrast media administration is urgently required for a patient with known untreated hyperthyroidism, the advice of an endocrinologist should be sought whenever possible prior to or following contrast media administration in patients with biochemical or clinical hyperthyroidism. Thyrotoxicosis generally occurs three to six weeks following iodinated contrast media administration. Emergency procedures can be performed if benefit outweighs risk and the patient can be appropriately monitored during this period.

R21. 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.

R22. Routine thyroid function testing of all patients with multinodular goitre prior to contrast media administration is not recommended.

R23. Patients who are to undergo diagnostic or therapeutic procedures involving radioisotope scanning of the thyroid (including thyroid cancer treatment) will have radioisotope uptake prevented for 8 weeks following iodinated contrast medai administration. This risk should be considered and weighed against the benefits of iodinated contrast media administration.

Myasthenia Gravis

R24. Symptoms of myasthenia gravis, including breathing difficulties, may be worsened by iodinated contrast media although the risk is thought to be low. Patients should be advised of the possibility of worsened symptoms prior to contrast media administration.

Phaeochromocytoma

R25. Direct intravascular injections of iodinated contrast media into adrenal or renal arteries or veins may precipitate a hypertensive crisis and should therefore be avoided in patients with known phaeochromocytoma, unless the patient is appropriately treated with alpha plus or minus beta blockers.

R26. No specific preparation is required prior to intravenous administration of iodinated contrast media in patients with a suspected phaeochromocytoma

Sickle Cell Disease

R27. There is no known serious medical risk associated with iodinated contrast media administration to patients with sickle cell disease. However, patients with sickle cell disease (homozygous HbS) should be advised that a small proportion of patients experience temporary worsening of pain following intravenous iodinated contrast media administration.
Interleukin-2 (IL-2) Therapy

R28. 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 a delayed anaphylactic contrast media reaction. No further precautions are required.

Breast Feeding

R29. Cessation of breast feeding or expression and discarding of breast milk after iodinated contrast media administration are not required.

Pregnancy

R30. Infants born to women who received iodinated contrast media while pregnant should have testing for hypothyroidism in the neonatal period. In Australia and New Zealand, this is routinely performed in every neonate via a heel prick test as part of formal newborn screening programs.

Intravenous Access and Contrast Media Extravasation

R31. A medical practitioner (ideally a radiologist) must be immediately available to attend to the patient in the event of an emergency or complication of iodinated contrast media administration and must be trained in recognising and treating severe contrast media reactions, including anaphylaxis, should be immediately available in the department where contrast media is administered.

R32. The task of obtaining intravenous access for administering intravenous contrast media can be performed by a medical practitioner (ideally a radiologist) or delegated to a suitably qualified healthcare professional trained and certified in cannulation for contrast media administration as per Appendix A of the RANZCR Standards of Practice for Diagnostic and Interventional Radiology. This training and certification may be performed by the radiology practice.

R33. The intravenous cannula should be left in place and the patient instructed to remain under supervision at the facility where contrast media has been administered for at least 15 minutes following contrast media injection. This period should be 30 minutes for patients at increased risk of an anaphylactic reaction.

R34. Extravasation of contrast media into the subcutaneous tissues is uncommon occurring in less than 1% of patients. Most injuries are minor and resolve without permanent injury with conservative treatment. Extravasation occurs more frequently with use of power injectors in comparison to hand injection of contrast media. Risk factors include use of small veins, fragile or previously damaged veins, obesity and large volume contrast media injections. The risk of contrast media extravasation can be reduced by use of an appropriately sized vein in relation to the contrast media injection rate and testing of the cannula with saline prior to contrast media administration. Where possible, direct visual monitoring of the injection site during the injection is advised.

R35. If contrast media extravasation occurs, conservative treatment with limb elevation, cold or warm compresses and monitoring for compartment syndrome is recommended. Surgical referral is required if serious injury such as cutaneous ulceration, tissue necrosis or compartment syndrome develop.
Training

R36. Healthcare practitioners and medical practitioners who administer intravenous contrast media shall be trained in the recognition of contrast media reactions, the procedures for treating these reactions, and resuscitation procedures.

R37. Suitably trained people who administer intravenous contrast media shall also be trained in basic life support including CPR, and in advanced life support where possible.

Contrast Media Administration

R38. Iodinated contrast media should be administered in accordance with the manufacturers’ product information and the TGA (in Australia) or Medsafe (in New Zealand) registration requirements. This applies to contrast media, contrast bottles/containers, syringes and all components of the delivery system. Radiologists and other health care practitioners who administer contrast media should be aware of relevant national guidelines for the safe administration of medication.

Emergency Equipment

R39. The following equipment must be readily available and within or nearby any room in which contrast media is to be injected (adult or paediatric sizes are optional for facilities that do not inject adult or paediatric patients, respectively):

a) Automated external defibrillator (AED)
b) Stethoscope, sphygmomanometer
c) Cardiac monitor
d) Pulse oximeter
e) Oxygen cylinders or wall-mounted oxygen source, flow valve, tubing, oxygen masks (adult and paediatric sizes if adult and paediatric patients are treated at the facility)
f) Suction: wall-mounted or portable; tubing and catheters
g) Oral and/or nasal airways: rubber/plastic
h) Bag and mask device; masks in adult and paediatric sizes; protective barriers for mouth-to-mouth respiration are optional if the bag-valve-mask device is stocked
i) Nebuliser equipment
j) Intravenous solutions (0.9% [normal] saline and IV tubing. 500ml or 1litre bags and also 10ml ampoules for mixing of IV medication
k) Syringes and IV cannulas: variety of sizes; tourniquets
l) Needles: Several sizes
m) Necessary medications:
   i. Adrenaline 1:1000, 1mg/mL
   ii. Atropine (eg. 1-mg in 10-ml preloaded syringe)
iii. Salbutamol inhaler with or without spacer  
iv. Salbutamol for nebuliser  
v. Hydrocortisone  
vi. Nitroglycerin (GTN) –, 0.4 mg tabs, sublingual  
vii. Glucagon 1-2mg IV  

n) Optional medications:  
i. Frusemide 20– 40 mg IV  
ii. Labetalol 20mg  
iii. Dextrose 50%  
iv. Antiemetic drugs e.g. ondansetron  
v. Aspirin (for chest pain where myocardial ischemia is a consideration)  

**Contrast Media Storage, Warming and Disposal**  

R40. Contrast media is to be stored in designated cupboards / shelving with clear separation of type, volume and density to prevent confusion.  

R41. Contrast media is to be stored away from direct sunlight.  

R42. Contrast media is to be stored away from radiation sources.  

R43. Contrast media is to be rotated as new orders arrive with new stock placed at the rear of the storage.  

R44. Contrast media is to remain stored in original packaging until being placed in a contrast media warmer or used.  

**Contrast Warmer**  

R45. Contrast media warmers should not be used for long-term storage of contrast media. Follow the manufacturer’s directions regarding storage.  

R46. Contrast media warmers should not be used for storing other products.  

R47. Contrast media warmers should be cleaned monthly.  

R48. Maximum and minimum temperatures of the contrast media warmer should be monitored.  

Major temperature variations should be reported to the quality manager (however named) and should be recorded in a temperature log. This is best done at the beginning of the day prior to door opening. The ideal temperature is 37°C.  

R49. Low turnover contrast media which risks being kept in the contrast media warmer for longer than 30 days should be clearly labelled with the date placed in the contrast media warmer.
**Disposal**

R50. Used plastic /vials/syringes/glass vials are to be disposed of safely and should comply with national or state/territory regulatory requirements.

R51. The unused portion of an opened contrast media syringe/vial is to be discarded according to national or state/territory regulatory requirements.

R52. Disposal of damaged or outdated contrast media comply with national or state/territory regulatory requirements which may include returning contrast media to the supplier or pharmacy.

**Patient Information and Consent**

R53. Fellows should be familiar with the RANZCR, Medical Imaging Consent Guidelines.

**Management of Anaphylactic Iodinated Contrast Media Reaction**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Signs/Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Mild Nausea / Vomiting</td>
<td>Supportive measures (antiemetics if prolonged vomiting)</td>
</tr>
<tr>
<td></td>
<td>Urticaria</td>
<td>Supportive measures</td>
</tr>
<tr>
<td></td>
<td>Urticaria (protracted)</td>
<td>Non-sedating antihistamine(s)</td>
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<tr>
<td>Moderate</td>
<td></td>
<td>Consider use of adrenaline 1:1000</td>
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<tr>
<td></td>
<td></td>
<td>• In adults: 0.1-0.25ml (0.1-0.25mg) intramuscularly into the anterolateral thigh – repeat as necessary</td>
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<td>• In children: 0.01mg/kg intramuscularly up to 0.3mg maximum dose</td>
</tr>
<tr>
<td></td>
<td>Bronchospasm or other</td>
<td>Keep supine; allow patient to sit if dyspnoeic</td>
</tr>
<tr>
<td></td>
<td>respiratory symptoms</td>
<td>Oxygen by mask (6-10 L/min).</td>
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<tr>
<td></td>
<td></td>
<td>Salbutamol or Terbutaline metered dose inhaler (2-3 deep inhalations)</td>
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<td>In more severe cases give Salbutamol or adrenalin by nebuliser.</td>
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<tr>
<td>Severity</td>
<td>Signs/Symptoms</td>
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</tbody>
</table>
| Moderate          | Bronchospasm or other respiratory symptoms  | Consider adrenaline  
• Normal blood pressure  
  o In adults: 1:1,000, 0.1-0.5 ml (0.1-0.5 mg) intramuscularly (use smaller dose in patients with coronary artery disease or elderly patients)  
  o In paediatric patients: 0.01 mg/kg up to 0.3 mg intramuscularly  
• Decreased blood pressure  
  o In adults: 1:1,000, 0.5 ml (0.5 mg) intramuscularly  
  o In paediatric patients: 0.01 mg/kg intramuscularly |
|                   | Hypotension                                 | Isolated hypotension  
• Keep supine; elevate patient’s legs  
• Oxygen by mask (6-10L/min)  
• Intravenous fluid: rapidly, normal saline or lactated Ringer’s solution  
  • If unresponsive: adrenaline: 1:1,000, 0.5 ml (0.5 mg) intramuscularly, repeat as needed |
|                   | Vaso-vagal reaction (hypotension and bradycardia) | Keep supine, elevate patient’s legs  
• Oxygen by mask (6-10L/min)  
• Atropine  
  o In adults 0.6-1.0mg intravenously, repeat if necessary after 3-5 min, to 3 mg total (0.04mg/kg).  
  o In paediatric patients give 0.02mg/kg intravenously (max. 0.6mg per dose) repeat if necessary to 2mg total.  
  o Intravenous fluids: rapid infusion of normal saline or Hartmann’s solution 20ml/kg, repeat as necessary |
| Severe            | Respiratory or circulatory collapse and/or seizures | Call for resuscitation team  
Keep supine. Allow patient to sit if dyspnoeic.  
Suction and maintain airway as needed  
Oxygen by mask (6 – 10L/min), ventilate patient if required |
<table>
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</tr>
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</table>
| Severe   | Respiratory or circulatory collapse and/or seizures | Intramuscular adrenaline into the anterolateral thigh  
- In adults (and in children greater than 25kgs), adrenaline 1:1000  
  less than 50 kg give 0.25 - 0.5 mL  
  greater than 50 kg give 0.5 mL  
- In children, Adrenaline 1:1,000  
  1 year 10kg give 0.1 mL  
  3 years 15kg give 0.15 mL  
  5 years 20kg give 0.2 mL  
  8 years 25kg give 0.25 mL  
- If necessary, repeat intramuscular dose every 5 minutes.  
- Large doses of adrenaline may be needed, up to a maximum of 5mL (5mg).  
- In adrenaline resistant cases, especially if the patient has taken beta blocking drugs, consider glucagon 1-2mg 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. normal saline 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: May be tried for laryngeal oedema (5ml of 1:1000)  
  Supportive measures  
  - Observe vital signs frequently; monitor ECG and pulse oximetry  
  - Arrange for transfer to hospital if reaction occurs in an outpatient facility  
  - Keep under observation for at least 4-6 hours after complete resolution of signs and symptoms, as biphasic reactions may occur |

R54. If a patient is suffering from a moderate or severe anaphylactic reaction additional extra care should be called for early.

R55. Adrenaline is potentially life-saving and must be used promptly. Withholding adrenaline due to misplaced concerns of possible adverse effects can result in deterioration and death of the patient.
R56. Adrenaline 1:1000 contains 1000 microgram in 1mL (1mg/mL). The volumes of adrenaline recommended for adults and children approximate to 5 to 10 microgram/kg. Children's weights are approximate for age. Repeated doses may be necessary.

R57. Adrenaline should be administered intramuscularly into the anterolateral thigh (vastus lateralis muscle). Administration into the deltoid muscle has been shown to result in a lower and slower rise in peak plasma adrenaline.

R58. Some cases are resistant to multiple doses of adrenaline, especially if the patient is taking beta blocking drugs. If adequate doses of adrenaline are not effective give glucagon 1 to 2mg intravenously over 5 minutes.

R59. Intramuscular adrenaline auto-injectors may have needle lengths which are inadequate to reach the vastus lateralis in overweight or obese patients (especially females). A suitable length needle should be used to ensure intra muscular administration into the vastus lateralis.

R60. Patients with moderate or severe reactions should be managed in a supine position to maximise circulation. If breathing is difficult, allow the individual to sit, but not stand. If vomiting or unconscious, lay the individual on their side in the recovery position. If hypotension is the sole or predominant problem, leg elevation may be useful.

R61. Emergency intubation for impending airway obstruction is a very high-risk procedure and should only be attempted by an expert.

R62. Corticosteroids may modify the overall duration of a reaction and may prevent relapse. However, onset of action will be delayed. Never use these to the exclusion of adrenaline.

R63. Patients who have experienced a reaction to contrast media should be provided with the exact name of the contrast media used and prompted to consider providing this detail in a MedicAlert bracelet.

**Oral and Other Non-Intravascular Contrast Administration**

R64. Anaphylactic reactions can occur with non-vascular administration of iodinated contrast media and the same precautions should be taken as with intravascular use.

R65. 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.

R66. Ionic contrast media should not be given orally to patients at risk of aspiration. Non-ionic contrast media or barium sulfate can be used as safer alternatives.