CHAPTER 22
MEDICINES USED FOR DIAGNOSIS

22.1 DIAGNOSTIC CONTRAST AGENTS AND RELATED SUBSTANCES

Medication used in diagnostic radiology includes:
Barium sulphate suspension.

- Non-ionic contrast media, e.g.:
  - iohexol, or
  - iopamidol, or
  - iopromide, or
  - ioversol.

SAFETY
The overall rate of adverse reactions is estimated to be less than 1 in 100[i] when using non-ionic contrast media and serious allergic reactions are even less common (about 1 in 2000[ii]). Contrast media-associated fatality is rare, estimated to be 2 per million injections.[iii]

Management of any reaction depends on it's severity. Life-threatening acute cardiopulmonary collapse should be treated according to guidelines for cardiopulmonary resuscitation. See chapter 20: Emergencies and injuries. Moderate and severe reactions may be associated with bronchospasm and wheeze, stridor, hypotension, and loss of consciousness. Stop the infusion of the contrast agent and start treatment as for anaphylaxis including adrenaline (epinephrine), oxygen (if indicated), intravenous fluids, and antihistamines. See sections 20.6: Angioedema and 20.7: Anaphylaxis/anaphylactic shock.

Iodine allergy: (Z91.0)
Patients allergic to iodine are at an increased risk of adverse drug reactions when exposed to iodine-containing contrast media and patients who report previous allergic reactions to contrast agents should be carefully evaluated as to the need for the investigation. If the investigation is considered essential, the patient should be pre-treated with steroids and antihistamines before proceeding.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 50 mg given 13 hours, 7 hours, and 1 hour before the procedure. *LoE:II*[iv]

Contrast-Induced Nephrotoxicity (CIN) is an important consideration; it may result in permanent renal impairment with significant effects on longevity. This is particularly important in an environment with limited access to renal replacement therapy. Before referring any patient for an

investigation involving contrast use, carefully weigh up the individuals' potential risk of CIN against potential benefits (the likelihood of detecting a condition for which a significant therapeutic intervention is available).

CIN is variously defined as either a 25% or a 50% rise on pre-contrast creatinine levels, or an absolute creatinine increase of more than 25 micromol/L. CIN is rare in individuals with normal renal function[v,vi] .

Factors that increase the risk of CIN include: diabetes, pre-existing renal impairment, age >75 years, anaemia, cardiac failure, hypotension and the volume of contrast media injected[vii,viii].

The probability of developing a 25% rise in creatinine after cardiac catheterisation in patients given 200 mL of non-ionic contrast media is linked to co-morbidity[vii]:

CIN risk	None	Anaemia	>75 yrs	CCF or low BP	>1 risk factor
No diabetes					
eGFR>60	7.5%	7.5%	7.5%	15%	15%
eGFR 40–60	7.5%	15%	15%	15%	15%
eGFR 20–40	7.5%	15%	15%	15%	25%
eGFR<20	15%	15%	25%	25%	25%
Diabetes					
eGFR>60	7.5%	15%	15%	15%	25%
eGFR 40–60	15%	15%	15%	25%	25%
eGFR 20–40	15%	25%	25%	25%	25%
eGFR<20	15%	25%	25%	25%	55%

The probability of needing dialysis after cardiac catheterisation is correlated with the risk of CIN[vii]:

CIN risk	7.5%	15%	25%	55%
Dialysis risk	0.04%	0.12%	1.1%	13%

Reducing the risk of developing CIN

There is no clear evidence that any specific medication is protective against the development of CIN. However, meticulous attention to fluid balance is important in patients at higher risk, as dehydration increases the risk of CIN.

Patients on metformin should be monitored for deterioration in renal function post procedure, as there is a small risk of precipitating lactic acidosis. In high risk patients it may be advisable to omit metformin for 48 hours after contrast injection while monitoring serum creatinine.

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Prednisone, oral: Tramèr MR, von Elm E, Loubeyre P, Hauser C. Pharmacological prevention of serious anaphylactic reactions due to iodinated contrast media: systematic review. BMJ. 2006 Sep 30;333(7570):675. https://www.ncbi.nlm.nih.gov/pubmed/16880193

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SOUTH AFRICAN ADULT HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 22: MEDICINES USED FOR DIAGNOSIS
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2017 - 2019)

Medicine amendment recommendations, with supporting evidence and rationale are listed below. Kindly review the medicine amendments in the context of this chapter.

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED
22.1 Diagnostic contrast agents and related substances	Ioversol 300	Deleted
	Ioversol 350	Deleted
-Iodine allergy	Prednisone, oral	Added (as a premedication)
	Cetirizine, oral	Not added (as a premedication)

22.1 DIAGNOSTIC CONTRAST AGENTS AND RELATED SUBSTANCES

Ioversol 300: *deleted*
Ioversol 350: *deleted*

The text was amended as follows, as the Adult Hospital Level Expert Review Committee was of the opinion that ioversol is non-ionic and water soluble, and should be grouped with the other agents:

Medication used in diagnostic radiology includes:
- Barium sulphate suspension.
- Non-ionic contrast media, e.g.:
  - iohexol, or
  - iopamidol, or
  - iopromide.
- ~~Ioversol 300 and 350.~~

Iodine allergy
Prednisone, oral: *added (as a premedication)*
Cetirizine, oral: *not added (as a premedication)*
The STG cautions about subjecting patients to investigations needing contrast only when absolutely essential and to uncertainties about the role of premedication (prednisone) in prophylaxis.
Level of Evidence: II Systematic review of low methodological quality, Guidelines

Prednisone, oral:
Systematic review[1] of 9 RCTs, to determine the efficacy of pharmacological prevention of potentially life threatening reactions to iodinated contrast media, were of poor methodological quality and suggested that life threatening anaphylactic reactions associated with iodinated contrast media are rare. RCTs were heterogenous and no RCTs analysis data using ITT analysis. Pooling of estimates was not possible due to differences in the type and dose of premedication and contrast media and the

[1] Tramèr MR, von Elm E, Loubeyre P, Hauser C. Pharmacological prevention of serious anaphylactic reactions due to iodinated contrast media: systematic review. BMJ. 2006 Sep 30;333(7570):675. https://www.ncbi.nlm.nih.gov/pubmed/16880193

authors reported a lack of data of premedication used in patients with a history of allergic reactions to iodinated contrast media.

Results (compared to placebo or no treatment):

- Respiratory symptom: 4/391 antihistamine cases vs 9/394 controls (OR 0.46, 0.15 to 1.39)
- Laryngeal oedema: In two trials, 3/778 methylprednisolone, oral/prednisolone, IV vs 11/769 controls (OR 0.31, 0.11 to 0.88; 2 RCTs; NNT=96).
- Composite outcome (shock, bronchospasm, and laryngospasm): 7/3093 methylprednisolone, oral vs 20/2178 controls (OR 0.28, 0.13 to 0.60; NNT=146).
- Angio-oedema: 1/196 IV clemastine and cimetidine vs 8/194 controls (OR 0.20, 0.05 to 0.76; 1 RCT; NNT=28).

The authors concluded that 'Physicians who are dealing with these patients should not rely on the efficacy of premedication'. They also suggest that as only a limited number of patients with serious reactions would have a positive skin test for the iodinated contrast media, radiology departments should be adequately trained to identify and treat anaphylactic reactions.

Guidelines: However, the above does show that corticosteroids are effective and standard practice[2] is to pre-medicate with oral corticosteroid in patients with a history of previous allergic reactions associated with contrast media.

Cetirizine, oral:

Systematic review[3]: Authors of a systematic review could not source RCTs testing combination of a steroid and antihistamine as pre-medication.

Report prepared by TD Leong: Secretariat to the Adult Hospital Level Committee (2017-2020)

- ***Note:*** *Information was sourced from NEMLC ratified minutes and NEMLC-approved documents.*

[2] American College of Radiology. ACR Manual on Contrast Media, 2018, version 10.3. https://www.acr.org/Clinical-Resources/Contrast-Manual

[3] Tramèr MR, von Elm E, Loubeyre P, Hauser C. Pharmacological prevention of serious anaphylactic reactions due to iodinated contrast media: systematic review. BMJ. 2006 Sep 30;333(7570):675. https://www.ncbi.nlm.nih.gov/pubmed/16880193