THE NORTHERN HOSPITAL

RADIOGRAPHIC IODINATED CONTRAST EMERGENCIES

Mae West, in "She Done Him Wrong", Paramount, 1933

HAT CHECK GIRL: *"Goodness what beautiful diamonds!"*

MAUDIE: *"Goodness had nothing to do with it dearie!"*

"Night After Night" Paramount 1932.

Mae West, a generation before Marilyn Monroe, was the original "blonde bombshell" of the silver screens of the 1920s and 1930s. Born in Brooklyn, New York City, 1893 she quickly developed into a precocious child prodigy as a vaudeville singer and actress. By the age of just fourteen, she had become known as the "child vamp". She was notorious for her razer sharp wit usually delivered, much to the delight of both female and male audiences, via racy sexual innuendo, astounding and quite shocking for its day. She became a prime target for the censors with her stage play entitled "Sex" in 1926 and was charged with obscenity, despite the fact that over 325,000 New Yorkers had stampeded to see it, including large numbers of the New York City Police Department and their wives. She was sentenced to 10 days in prison.

Famous as Mae was on the stages of New York City, in 1932 she was catapulted to international stardom (and notoriety) when she displayed her sultry "talents" and wise-cracking repartee in "Night After Night", her first role on the big silver screen. She played the relatively minor role of Maudie Triplett, but it was her ability to cut to the chase with racy one-liners that made her an instant sensation. She was angry over her small role in Night After Night, but such was her visual presence on the big screen she was appeased by allowing her to rewrite her own scenes! George Raft, who played the starring role in the film later reflecting on her rewritten scenes, remarked, "She stole everything but the cameras!"

She was known for her passion for diamonds - and she never got her priorities confused over these. She once quipped "I never worry about diets. The only carrots that interest me are the number you get in a diamond!" Her possibly most famous role came in 1933 when she starred as "Diamond Lil" alongside another fast rising star - Cary Grant.

When we need to give contrast to our patients who need time critical CT scans there must be no unnecessary delay.

We must like Ms West "cut to the chase" and not confuse our priorities - in potentially life threatening emergencies our diamond is emergent CT scanning and the eGFR will have "nothing to do with it!"

RADIOGRAPHIC IODINATED CONTRAST EMERGENCIES

Introduction

Injection of **iodinated radiographic contrast media** is generally safe, however with increased use adverse events may be more likely to occur.

The most important potential adverse effects include:

1 **Hypersensitivity reactions**

2 **Contrast-induced nephropathy (CIN)**

3. **Metformin induced lactic acidosis in patients with renal impairment**

4. **Thyrotoxicosis**

See also separate documents on:

- **Anaphylaxis (in Allergy folder)**
- **Acute Renal Impairment (in Renal & Electrolytes folder).**

HYPERSENSITIVITY REACTIONS

Introduction

Hypersensitivity reactions to iodinated contrast media can be classified into:

- Immediate anaphylactic reactions
- Delayed reactions.

Risk Assessment

1. Non-ionic, low osmolar versus ionic high osmolar media:
    - The current non-ionic, low osmolar iodinated contrast media are in the order of 5 - 10 times safer, in terms of mild to moderate reactions, than the older, high osmolar ionic media.
2. Previous hypersensitivity reaction:
    - There is an approximate tenfold increase in reactions to both ionic and non-ionic contrast media following a previous hypersensitivity reaction.
3. Asthma:

- Patients with a history of **asthma** experience an approximate six-fold increased risk of a hypersensitivity contrast media reaction.

  The risk of reaction appears related to the degree of control of a patient's asthmatic symptoms with the risk highest in patients with unstable disease.

4. A history of multiple allergies:

   - A history of multiple allergies requiring medical treatment is associated with a 3 - 5 fold increase in the risk of an acute reaction to iodinated contrast media.

     Most such reactions are mild.

Shellfish allergy is **not** associated with an increased risk of adverse reaction to intravenous iodinated contrast media, over and above the approximate 3-fold increased risk associated with other food allergies in general.

Skin irritation or "allergy" to topical iodine antiseptic solutions is **not** associated with an increased risk of adverse reaction to intravenous iodinated contrast media.

Clinical Features

Immediate anaphylactic reactions:

The RANZCR has classified immediate reactions as:

1. Mild:

   These reactions are usually self-limited and resolve without specific treatment.

   They may be seen in up to 1% of patients after non-ionic low-osmolality contrast media administration.

   Clinical features include:

   - Flushing
   - Nausea
   - Pruritus
   - Vomiting
   - Headache
   - Minor urticaria.

2. Moderate:

- Severe vomiting
- Marked urticaria
- Bronchospasm or other respiratory symptoms
- Facial/laryngeal oedema
- Syncope

3. Severe:

Severe / life-threatening anaphylactic reactions are uncommon, occurring in less than 1 in 100,000 patients.

Clinical features include

- Shock
- Respiratory arrest/ Cardiac arrest
- Convulsions.

Delayed reactions:

Delayed contrast media reactions occur between **1 hour - 1 week** after intravascular iodinated contrast media administration.

These are typically skin reactions which can include:

- A maculopapular rash (most commonly).
- Angioedema
- Urticaria

Delayed hypersensitivity reactions are **not** typically associated with bronchospasm or laryngeal oedema.

The incidence of reported delayed sensitivity reactions varies in the literature but is likely to be around 4% or less.

There may be an increased incidence of late reactions to iodinated contrast media in patients who have received interleukin-2 (IL-2).

The effectiveness of premedication with corticosteroids in reducing the incidence of recurrent delayed hypersensitivity contrast media reaction is unknown.

Management

In patients who are at increased risk of an anaphylactic reaction to iodinated contrast media but require a contrast study, the risk including the severity of any previous reaction, has to be weighed against the possible benefit.

Strategies include:

1. 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).

2. 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:

    - 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

    - Maintain close medical supervision and ensure emergency drugs and equipment for resuscitation are readily available

    - Leave the cannula in place and keep the patient under observation for at least 30 minutes after contrast media administration

3. Premedication:

    While safe for the majority of patients, the medical literature supporting the routine use of premedication in patients with a prior contrast media reaction is limited.

    Several older studies have shown premedication with steroids or antihistamines reduce the risk of anaphylactic reactions to ionic contrast media.

    There is as yet **no** convincing evidence that premedication with corticosteroids and/or antihistamines reduces the incidence of severe acute reactions, including death, to non-ionic contrast media.

    The RANZCR recommends for semi -elective situations:

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

    A typical premedication regimen for adults is:

    - Prednisolone 50mg orally, given at 13 hours and 1 hour before contrast media administration.

- Oral non-sedating antihistamines may be added to the above premedication regimen.

The above regimen, however is of course, no use in the Emergent situation.

Should an anaphylactic reaction occur, treatment is along usual lines for this, (see also separate document on Anaphylaxis in Allergy folder).

Oral Contrast and Allergic reactions

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 **very rare**, precautions should be taken as with intravascular administration.

Ionic contrast media should not be given orally to patients:

- At risk of aspiration
- Unable to tolerate oral fluids, due to nausea and vomiting.

IV - CONTRAST INDUCED NEPHROPATHY (CIN)

Introduction

Since the previous version of the **RANZCR Guidelines for Iodinated Contrast Administration (2009**), a *substantial* amount of new evidence regarding the causal relationship, **if any**, between intravenously administered iodinated contrast media and contrast induced acute kidney injury (CI – AKI) has accumulated.

The American College of Radiology Manual on Contrast Media V10, 2015 and the current European Society of Uro-radiology Guidelines have revised their previous advice about the severity of renal function impairment that is associated with an increase in the risk of CI – AKI.

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, increased risk of dialysis or death related to the development of AKI.

In the past our understanding of contrast-induced nephropathy was largely informed by studies that predated the use of low-osmolar and iso-osmolar contrast agents

In the largest well-controlled study of acute kidney injury following contrast administration in the ED to date, by Jeremiah S. Hinson at al , intravenous contrast was *not* associated with an increased frequency of acute kidney injury. [5]

An editorial by Daniel J. Pallin on this study concluded: "If contrast-enhanced CT is essential for ruling out a serious condition and no alternative test is readily available, this study should reassure emergency physicians and radiologists to proceed with the scan, even in patients with creatinine levels as high as 4 mg/dL, (i.e 353.6 micromols / L)

If a patient has an elevated creatinine after contrast-enhanced CT, a *causal relationship should not be assumed*, and the providers who ordered and performed the study in good faith should not be faulted"

Classification of Iodinated Contrast Media

Iodine-based agents are compounds of 2, 4, 6 tri-iodobenzoic acid.

Iodinated contrast media are classified as:

1. Non-ionic:
    - Low osmolality (non-ionic monomers, non-ionic dimers).
2. Ionic:
    - High osmolality (ionic monomers)

- Low osmolality, (ionic dimers)

The osmolality, viscosity and iodine content of contrast media are closely interrelated.

Adverse effects increase with **higher osmolality.**

Iodine content is **not** an independent indicator of adverse events.

The non-ionic dimers are preferred due to lower osmolality and less chemotoxicity. However they are more viscous than non-ionic monomers, and more expensive.

Risk Assessment

(Supposed) risk is now stratified from lowest to highest as follows:

eGFR	**Risk Level**
> 45 mL/min	No risk
30-45 mL/min	Low risk
< 30 mL/min	Some risk
Patient on dialysis	Not applicable

Investigation

Even in **elective** situations, not all patients undergoing procedures involving intravenous iodinated contrast media administration require formal testing of their renal function prior to contrast media administration.

Severe renal function impairment that ideally should be identified prior to iodinated contrast media administration is **rare** in patients who are unaware that they have either diabetes or kidney disease.

The AusDiab Study established that the frequency of undiagnosed severe (eGFR less than 30ml/min/1.73m^2) renal function impairment in Australian adults aged over 25 years was less than 1%.

Many risk factors have been thought to be associated with subsequent CI-AKI but current guidelines do not agree on which ones should result in pre-contrast media renal function testing, with the *exception* of **known kidney disease** and **diabetes**.

Furthermore, as the occurrence of severe renal impairment that the patient is unaware of is very uncommon, the usefulness of asking patients about large numbers of risk factors to identify a very small proportion of patients with clinically important renal impairment is not clear.

The larger the number of screening questions, the more patients have renal function testing that does not contribute to decision making about contrast media administration or peri-procedural hydration, and this adds to healthcare costs without patient benefit.

The following are generally agreed risk factors that require eGFR testing in non-emergent situations:

1. Known kidney disease (including kidney transplant)

2. Presence of diabetes

3. Taking metformin.

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

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.

Management

RANZCR makes the following 5 recommendations:

1. **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.**

   These situations time critical investigation required to potentially save life or significant morbidity

2. **Emergency imaging procedures requiring contrast media administration should not be delayed in order to obtain renal function testing results prior to the procedure.**

   Examples include:

   - **Angiography in PCI amenable ACS**

- **Stroke, within intervention time frames.**
- **Acute bleeding**
- **Significant trauma**
- **Suspected massive pulmonary embolism**
- **Suspected acute aortic dissection**

3. **eGFR > 45 mL/min/1.73m^2:**

   - **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/1.73m^2.**

     ***No* special precautions are recommended in this group prior to or following intravenous administration of iodinated contrast media.**

4. **eGFR 30 - 45 mL/min/1.73m^2:**

   - **The risk of intravenous CI-AKI is also very likely to be low or non-existent for patients with eGFR 30 - 45 mL/min/1.73m^2.**

     Universal use of *peri-procedural hydration* in this group to prevent the theoretical risk of CI-AKI *cannot* be recommended.

     However patients with impaired function in this range that is *acutely deteriorating* rather than stable may benefit from this intervention.

5. **eGFR < 30 mL/min/1.73m^2:**

   - **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 peri-procedural renal protection using intravenous hydration with 0.9% saline.

     However, severe renal function impairment should *not* be regarded as an *absolute* contraindication to medically indicated iodinated contrast media administration.

Hydration procedure:

In cases where **hydration** is to occur the following is noted:

1. Oral peri-procedural hydration **cannot** be recommended as a substitute for the intravenous administration route based on lack of demonstrated efficacy.

   This may relate to variable absorption / administration of oral fluids and lack of standardisation of an administration regimen.

2. There is no evidence to support a specific volume or duration of pre and post procedural hydration due to heterogeneity of the published studies.

The exact administration rate will also depend on, amongst other things, the patient's pre-test risk of **cardiac failure / pulmonary oedema** as a result of intravenous administration of normal saline.

- **0.9% intravenous saline, 1.0 - 1.5 ml/kg/hour, for at least 6 hours before and after contrast media injection in elective cases**

  In emergency cases fluid can be commenced concurrently with the IV contrast CT exam and continued for 6 hours afterwards.

There is **no** clear evidence in support of the additional benefit of **N-acetyl cysteine** and/or **sodium bicarbonate** alone or in combination with intravenous 0.9% saline and currently these additional measures are **not recommended**.

METFORMIN INDUCED LACTIC ACIDOSIS IN RENAL IMPAIRMENT

IV Contrast:

Patients receiving intravenous iodinated contrast media with an eGFR above **30 ml/min/1.73 m^2** should **continue taking metformin.**

Patients with an **unknown recent eGFR** or an **eGFR less than 30 ml/ min/1.73 m^2**, 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 Contrast:

Patients undergoing an intra-arterial procedure requiring iodinated contrast media with an eGFR above **45 ml/min/1.73 m^2** 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 an eGFR less than 45 ml/ min/1.73 m^2, or who are unwell or have deteriorating renal function should cease metformin for at least 48 hours following intra-arterial administration of contrast media and have an eGFR estimated prior to restarting metformin.

THYROTOXICOSIS

Introduction

Patients with **clinical *or* biochemical** evidence of hyperthyroidism prior to iodinated contrast media administration are at risk of developing clinical hyperthyroidism and / or acute thyrotoxicosis.

Patients with **normal thyroid function** or **treated hyperthyroidism** that is medically controlled are at **low risk** of developing clinically important or sustained hyperthyroidism following iodinated contrast media administration.

Management

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 **3-6** 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.

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 media administration. This risk should be considered and weighed against the benefits of iodinated contrast media administration.

Appendix 1

The Chemistry of Iodine:

Iodine, (from Iodes or violet) Life Science Library, "Matter", 1963.

Elemental symbol:	**I**
Atomic number	53
Atomic weight.	126.90447
Classification	Non-metal
Physical appearance	Violet - grey lustrous solid.
Melting point:	113.7 °C
Boiling point:	184.3 °C.
Discovered by:	Barnard Courtois in 1811

References

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