What I tell my patients about contrast medium nephrotoxicity

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Contrast media are colourless solutions, which are used to assist in diagnostic and interventional procedures such as X-rays with dye, angiography (which is used to outline blood vessels, see Figure 1), computed tomography (CT) scans and magnetic resonance imaging (MRI). These contrast media can occasionally cause kidney damage, especially in patients who already have kidney disease. Contrast media are of different types, some of which are more 'kidney-friendly' than others.

Contrast medium nephrotoxicity (kidney toxicity that arises from the use of contrast media) is a form of kidney failure that leads to worsening of a patient's kidney function tests by more than 25% from baseline within three to four days after the use of a contrast medium, in the absence of another cause for such failure.

Contrast medium nephrotoxicity is a rare problem and this is why it is often under-recognised in clinical practice. The kidney injury is usually temporary and reversible, but in some patients dialysis may be necessary, and in rare cases, the injury could be permanent.

Nonetheless, contrast medium nephrotoxicity is important to recognise, as it increases the risk of kidney damage and the length of hospital stay for the patient. It also increases the incidence of other complications, such as infections, heart disease and delayed wound healing. To date, there has been no effective treatment found for contrast medium nephrotoxicity.

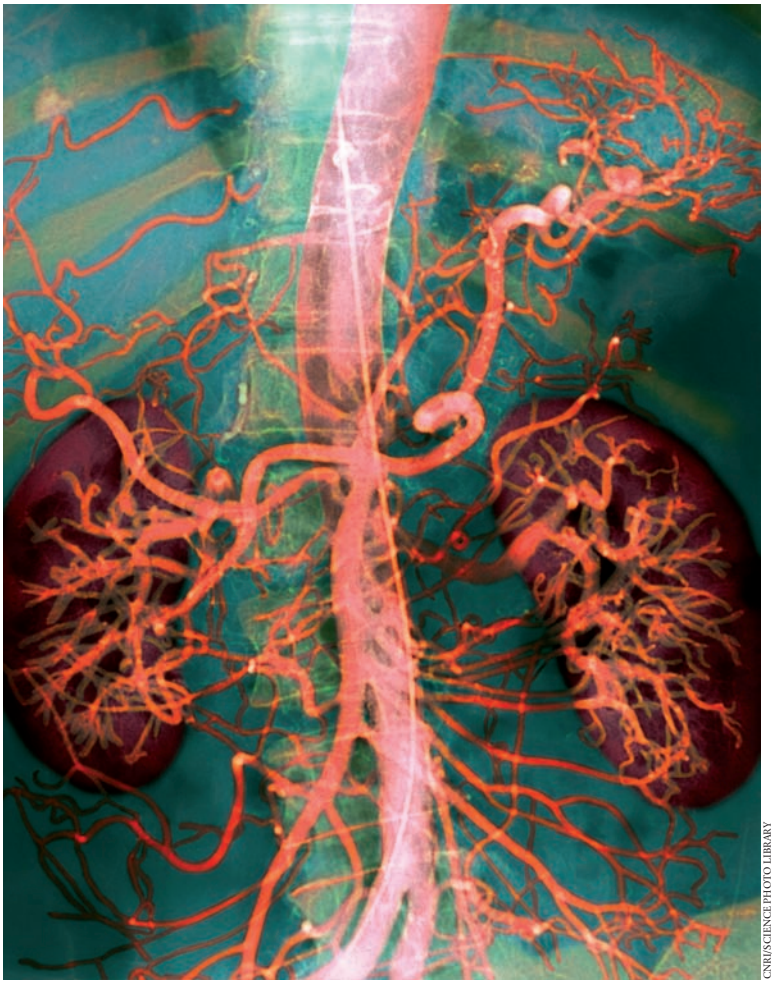

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Figure 1. A coloured angiogram of the arteries of the abdomen, showing the kidneys. The contrast medium that is used to reveal blood vessels on angiography can sometimes have a damaging effect on the kidneys – what is known as contrast medium nephrotoxicity

How common is contrast medium nephrotoxicity?

Contrast medium nephrotoxicity is rare in people with normal kidney function, varying from 0–5%. However the frequency of the condition increases to 12–27% in people who already have abnormal kidney function.

In clinical practice, contrast medium nephrotoxicity may be underestimated because serum creatinine measurement, which is the test used to assess kidney function, is an insensitive test when it is used on its own, as it does not show early abnormality when kidney damage starts.

Estimated glomerular filtration rate (eGFR) is a more accurate measure of kidney function. The glomeruli are small bundles of capillaries in the kidneys that form part of the system that filters the blood, and so their rate of filtration is a

Box 1. Managing the risk of contrast medium nephrotoxicity

Risk factors for contrast medium nephrotoxicity

- Patients who already have abnormal kidney function (serum creatinine >130 µmol/l or estimated glomerular filtration rate below <60 ml/min)
- Diabetes
- Dehydration
- Heart failure
- Old age
- High uric acid levels
- Multiple myeloma (abnormal production of proteins by the bone marrow)
- Use of other drugs that may potentially damage the kidney, such as anti-inflammatories (eg ibuprofen, dicoflenac), or some antibiotics (eg gentamicin)

Contrast media-related risk factors

- Dose: injection of a large dose of contrast media
- Type: use of 'kidney-unfriendly' types
- Multiple administrations of contrast media
- Administration of contrast media into the arteries rather than veins

Box 2. How can contrast medium nephrotoxicity be avoided?

- Consider an alternative imaging method not using contrast media
- Identify patients at high risk (as in Box 1) and inform the renal department
- Good hydration of patients six to 12 hours before and after being given the contrast media, with administration of fluids into the veins. This regimen is suitable for patients who are not in heart failure, in such patients oral fluid may be more appropriate if they are allowed to drink. At least 500 ml of water or soft drinks before and 2,400 ml during the following 24 hours should be offered orally
- Stop drugs that could potentially increase kidney damage, such as anti-inflammatories, diuretics (water tablets), or angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (eg ramipril, losartan)
- N-acetylcysteine is an antioxidant that may offer protection against contrast medium nephrotoxicity in patients with abnormal kidney function. This drug can be offered before administration of the contrast media, according to the protocol of the individual radiology department
- Use of 'kidney-friendly' types of contrast media
- Injection of small volume of contrast medium (less than 100 ml)
- Avoiding short intervals (under 48 hours) between procedures requiring administration of contrast media

measure of how well the kidney is functioning; eGFR indicates significant kidney damage when it drops below 60% of normal.

Another reason why contrast medium nephrotoxicity is rare in clinical practice is that patients rarely undergo kidney function tests either before or after procedures where contrast media have been used.

What is the outcome of contrast medium nephrotoxicity?

Most cases of contrast medium nephrotoxicity are self-limited and resolve within one to two weeks. Only 1% of contrast medium nephrotoxicity episodes require dialysis and permanent kidney damage is rare.

The interaction of metformin with contrast media

Metformin is a drug used as an antidiabetic treatment. Approximately 90% of metformin is removed through the kidneys.

Kidney failure will cause retention of metformin in the tissues and may then lead to the build up of acid levels in the body. This is a condition known as lactic acidosis.

The use of contrast media in patients taking metformin should be carried out with care. Contrast media can cause kidney failure, which occurs after the contrast medium has reached the kidney, leading to retention of metformin that may then induce lactic acidosis. This complication has almost always been observed in diabetic patients who had abnormal kidney function before injection of contrast media.

If serum creatinine is raised >130 µmol/l or eGFR is below 60 ml/min, metformin should be withheld for 48 hours before and 48 hours after the contrast media is given, and kidney function should be reassessed before restarting the use of metformin.

What should happen after contrast medium has been used?

After diagnostic tests that use a contrast medium have taken place, patients who are at risk (see Box 1) should have their kidney function measured within seven days.

It is especially important that this be undertaken in patients:

- Who have diabetes and/or are taking metformin
- Who have received contrast medium into the arteries (rather than the veins)
- Who have previously had abnormal kidney function tests or who have a history of kidney disease
- Who have had kidney surgery
- Who have high blood pressure, gout or protein leak in the urine (proteinuria)

Table 1. What do patients already on dialysis need to do when they receive contrast media?

Patients on haemodialysis	Recommendations
• Usually the kidneys are already damaged and there is no concern about nephrotoxicity. • However, if there is residual renal function, please refer to Box 2	• Hydration in unnecessary and may lead to fluid overload • Correlation of the time of contrast media injection with the haemodialysis session is unnecessary • Extra haemodialysis session for removal of contrast media is unnecessary. However, a haemodialysis session shortly after magnetic resonance imaging (MRI) with gadolinium contrast is recommended
Patients on continuous ambulatory peritoneal dialysis (CAPD)	**Recommendations**
• All contrast media can be removed by peritoneal dialysis	**Radiography studies, computed tomography (CT) scans** • To protect residual renal function, please refer to Box 2 • Hydration should be considered only after careful evaluation of fluid balance of the patient • Haemodialysis is not recommended **MRI** • To protect residual renal function, use only small doses (up to 0.3 mmol/kg of body weight) of gadolinium-based contrast agents • Haemodialysis is not recommended • Several rapid peritoneal dialysis exchanges after use of gadolinium contrast MRI are advised

- Who have recently used drugs that could potentially damage the kidney.

There are precautions that can be taken to avoid inducing contrast medium nephrotoxicity in patients who are at risk of developing the condition (see Box 2). While haemodialysis removes contrast medium effectively, there is no evidence that haemodialysis before or after use of contrast medium reduces nephrotoxicity.

What is nephrogenic systemic fibrosis?

Nephrogenic systemic fibrosis is a new and rare debilitating condition also known as nephrogenic fibrosing dermopathy. The first case was identified in 1997 in the USA. Patients develop scar tissue, and thickening and tightness of skin of the limbs, trunk (see Figures 2 and 3), joints and eyes; internal organs such as the liver, lungs, muscles and heart may be also involved.

It occurs in a minority of patients with chronic kidney disease (either before starting dialysis or already on dialysis) after exposure to contrast media containing gadolinium used in MRI studies. MRI is primarily a medical imaging technique most commonly used to visualise the internal structure and function of the body. MRI provides much greater contrast between the different soft tissues of the body than CT scanning (see Figure 4).

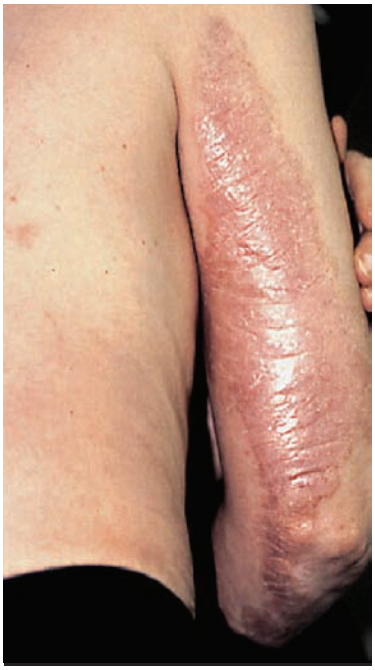

Figure 2. Nephrogenic systemic fibrosis affecting the rear of the arm

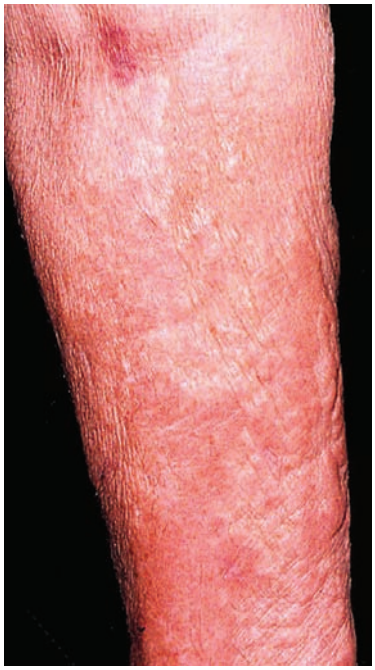

Figure 3. Nephrogenic systemic fibrosis affecting the inner arm

The condition may develop over a period of days to a few months after exposure to gadolinium. In many cases, the skin thickening prevents movement and bending of joints, resulting in contractures and disability. Muscle weakness is a common feature. Approximately 5% of patients have a rapidly progressive course that may rarely result in death from

Box 3. Useful websites

- www.esur.org/ESUR_Guidelines_NEW.6.0.html (European Society of Urogenital Radiology guidelines to avoid contrast medium nephrotoxicity)
- www.icnfdr.org (Official site of The International Center for Nephrogenic Fibrosing Dermopathy Research)

complications. The natural history of the disease and the reasons behind contracting it are not, as yet, well understood. Some patients report a gradual improvement in mobility and slight softening of the skin over time.

How can nephrogenic systemic fibrosis be avoided?

Although many treatments have been tried, it seems that there is no consistently successful treatment for nephrogenic systemic fibrosis. Avoiding the administration of contrast media containing gadolinium in patients with advanced chronic kidney disease (eGFR<30 ml/min) is the main preventative strategy, unless it is clinically essential for diagnosis.

Patients with advanced kidney disease and those on dialysis who need MRI studies should receive a more stable contrast medium that is less likely to release gadolinium. The lowest possible amount of contrast should be used and should not be repeated within a week. Patients on dialysis should be scheduled to have either their regular haemodialysis session, or several rapid exchanges if they are on peritoneal dialysis, shortly after the MRI examination ■

Key points

- **Contrast media do not usually cause any problems. They can, however, in rare cases, cause unwanted effects in some people, especially those who already have kidney disease.**
- **Contrast medium nephrotoxicity is a problem that is often under-recognised in clinical practice. It is costly, prolonging hospital stay and potentially necessitating dialysis.**
- **The burden of contrast medium nephrotoxicity could be reduced by identifying at-risk patients. In these patients, adequate hydration is required, the contrast dose should be minimised and contrast agents with a more favorable renal profile are recommended.**
- **The awareness of the potential adverse reactions associated with contrast media and the necessary precautions to take are of utmost importance both for radiologists and referring nephrologists.**

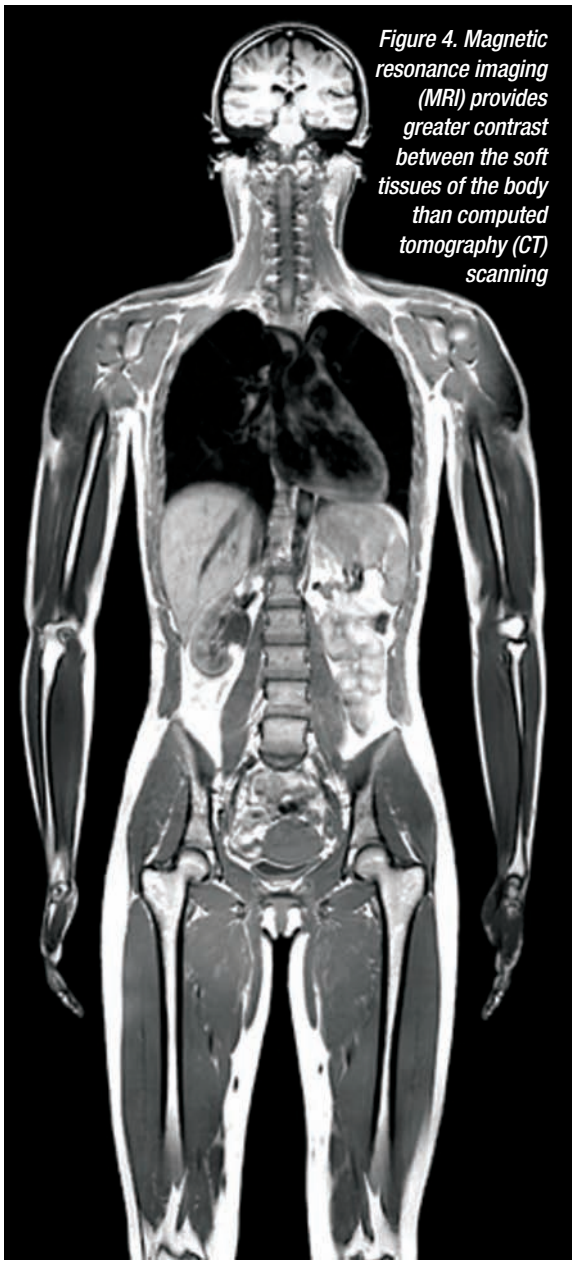

Figure 4. Magnetic resonance imaging (MRI) provides greater contrast between the soft tissues of the body than computed tomography (CT) scanning

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