Bronchography (examination of the bronchial tree) has been performed with oily or aqueous media, such as iopydol or iopydone, instilled through a catheter or bronchoscope to coat the airways; however, other visualisation techniques are generally preferred.

For **hysterosalpingography** (visualisation of the uterus and fallopian tubes) ultrasound and endoscopic techniques are generally used, and microbubble contrast media such as galactose may be used to improve ultrasound images. If radiography is performed, water-soluble iodinated contrast media may be used.

For **lymphography** or **lymphangiography** (visualisation of the lymphatic system) a high radiodensity is required and the contrast medium must be retained within the lymphatic system for long enough to be visualised, requiring particulate, water-insoluble media, or very large molecules. Iodised oil has been most widely used, but adverse effects and limited distribution within the lymphatic system restrict its use.

Adverse effects of contrast media. Although contrast media are generally considered to be very safe, with most adverse effects being mild and transient, more severe and even life-threatening reactions are possible, and the risk of adverse effects may influence the choice of contrast medium or imaging technique in a particular patient.

Iodinated radiographic contrast media all have a similar range of adverse effects (see under Amidotrizoic Acid, p.1475) but the incidence and severity varies. Many of the adverse effects are related to the osmolality of the preparation, and the incidence tends to be lower with those that have low osmolality. Osmolality depends on the number of particles present in the solution; for a given iodine content, this is highest for the ionic monomers and lowest for nonionic dimers, and this is reflected in the incidence of adverse effects. Hypersensitivity reactions also tend to be less frequent with nonionic media (see under Amidotrizoic Acid, p.1476), although these reactions are not directly related to osmolality. However, low-osmolality media tend to be more expensive; while nonionics and dimers are preferred, ionic monomers may still have a role in patients at low risk of adverse effects. Ionic contrast media may also carry a lower risk of thromboembolism (see Effects on the Blood, p.1476).

Magnetic resonance contrast media tend to be safer than iodinated contrast media, although similar general effects may occur. Ionic and nonionic media are available, but this tends to have little influence on the incidence of adverse effects. All gadolinium chelates have similar adverse effects (see under Gadopentetic Acid, p.1479); there is a theoretical risk of gadolinium toxicity due to instability of the chelates and most preparations also contain free chelating agent to reduce this risk. The adverse effects of superparamagnetic iron compounds are described under ferumoxides (p.1478) and ferumoxsil (p.1478).

Ultrasound contrast media are generally safe; minor and transient adverse effects have been reported, but may be due to the procedure rather than to the contrast medium used.

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2. Runge VM. Safety of approved MR contrast media for intravenous injection. *J Magn Reson Imaging* 2000; **12:** 205–13.
3. Maddox TG. Adverse reactions to contrast material: recognition, prevention, and treatment. *Am Fam Physician* 2002; **66:** 1229–34.
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6. Jakobsen JÅ, *et al.* Safety of ultrasound contrast agents. *Eur Radiol* 2005; **15:** 941–5.
7. Morcos SK. Acute serious and fatal reactions to contrast media: our current understanding. *Br J Radiol* 2005; **78:** 686–93.
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9. European Society of Urogenital Radiology. ESUR guidelines on contrast media (February 2007). Available at: http://www.esur.org/fileadmin/Guidelines/ESUR_2007_Guideline_6_Kern_Ubersicht.pdf (accessed 14/07/08)

Adipiodone *(BAN, rINN)*

Adipiodon; Adipiodona; Adipiodoni; Adipiodonum; Iodipamide. 3,3′-Adipoyldiaminobis(2,4,6-tri-iodobenzoic acid).

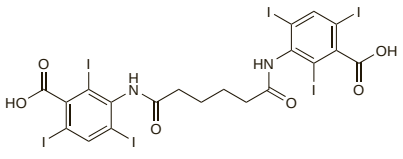
Адипиодон

$C_{20}H_{14}I_6N_2O_6$ = 1139.8.

CAS — 606-17-7.

ATC — V08AC04.

ATC Vet — QV08AC04.



Description. Adipiodone contains about 66.8% of I.

Pharmacopoeias. In *Chin.* and *US.*

USP 31 (Iodipamide). A white, practically odourless, crystalline powder. Very slightly soluble in water, in chloroform, and in ether; slightly soluble in alcohol. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Meglumine Adipiodone *(rINNM)*

Adipiodona de meglumina; Adipiodone Méglumine; Adipiodone Meglumine *(BANM)*; Dimeglumine Iodipamide; Iodipamide Meglumine; Meglumine Iodipamide; Meglumini Adipiodonum. The di(*N*-methylglucamine) salt of adipiodone.

Меглумина Адипиодон

$C_{20}H_{14}I_6N_2O_6.(C_7H_{17}NO_5)_2$ = 1530.2.

CAS — 3521-84-4.

ATC — V08AC04.

ATC Vet — QV08AC04.

Description. Meglumine adipiodone contains about 49.8% of I.

Pharmacopoeias. *US* includes only as an injection.

Incompatibility. Incompatibilities have been reported between meglumine adipiodone and some antihistamines.

Adverse Effects, Treatment, and Precautions

See under the amidotrizoates, p.1475. Rapid injection may increase the incidence of adverse effects.

Adipiodone may show some uricosuric activity.

Effects on the liver. Of 149 patients given the recommended dose of adipiodone, 13 developed elevated serum aspartate aminotransferase (SGOT) values; of 126 who received twice the dose, 23 developed elevated values.[1] Hepatotoxicity has also been reported[2-4] on isolated occasions in patients given meglumine adipiodone.

1. Scholz FJ, *et al.* Hepatotoxicity in cholangiography. *JAMA* 1974; **229:** 1724.
2. Stillman AE. Hepatotoxic reaction to iodipamide meglumine injection. *JAMA* 1974; **228:** 1420–1.
3. Sutherland LR, *et al.* Meglumine iodipamide (Cholografin) hepatotoxicity. *Ann Intern Med* 1977; **86:** 437–9.
4. Imoto S. Meglumine hepatotoxicity. *Ann Intern Med* 1978; **88:** 129.

Pharmacokinetics

Meglumine adipiodone is rapidly distributed in extracellular fluid after intravenous injection and is reported to be extensively bound to plasma proteins. It appears in the bile ducts within about 10 to 15 minutes after injection, with peak opacity at about 20 to 30 minutes, and reaches the gallbladder by about 1 hour, peak opacification occurring after about 2 hours. About 80 to 95% is excreted unchanged in the faeces; small amounts are excreted unchanged in urine. A terminal half-life of about 2 hours has been reported.

Uses and Administration

Adipiodone is an ionic dimeric iodinated radiographic contrast medium (see p.1474); it is taken up by the liver and excreted in bile, and is used in cholangiography and cholecystography.

Adipiodone is given intravenously as a solution containing 52% of the meglumine salt. The usual dose is about 10 g of meglumine adipiodone, given by slow intravenous injection over about 10 minutes.

A solution of meglumine adipiodone with meglumine diatrizoate is given by intra-uterine instillation for hysterosalpingography.

Preparations

BP 2008: Meglumine Iodipamide Injection;
USP 31: Iodipamide Meglumine Injection.

Proprietary Preparations (details are given in Part 3)

USA: Cholografin.

Multi-ingredient: ***USA:*** Sinografin.

Amidotrizoic Acid *(BAN, rINNM)*

Acide amidotrizoïque; Ácido amidotrizoico; Acidum amidotrizoicum; Acidum Diatrizoicum; Amidotritsoiinihappo; Amidotrizoesav; Amidotrizoinė rūgštis; Amidotrizoinsyra; Diatritsoiinihappo; Diatrizoic Acid *(USAN)*; Diatrizoinsyra; Kyselina amidotrizoová; NSC-262168. 3,5-Diacetamido-2,4,6-tri-iodobenzoic acid.

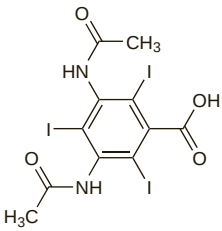
Амидотризоевая Кислота

$C_{11}H_9I_3N_2O_4.2H_2O$ = 649.9.

CAS — 117-96-4 (anhydrous amidotrizoic acid); 50978-11-5 (amidotrizoic acid dihydrate).

ATC — V08AA01.

ATC Vet — QV08AA01.



Description. Amidotrizoic acid contains about 62% of I calculated on the anhydrous substance.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*

Ph. Eur. 6.2 (Amidotrizoic Acid Dihydrate). A white or almost white, crystalline powder. Very slightly soluble in water and in alcohol; dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Diatrizoic Acid). It is anhydrous or contains two molecules of water of hydration. A white, odourless, powder. Very slightly soluble in water and in alcohol; soluble in dimethylformamide and in alkali hydroxide solutions.

Meglumine Amidotrizoate *(BANM, rINNM)*

Amidotrizoate de Méglumine; Amidotrizoato de meglumina; Diatrizoate Meglumine; Meglumine Diatrizoate; Meglumini Amidotrizoas; Methylglucamine Diatrizoate. *N*-Methylglucamine 3,5-diacetamido-2,4,6-tri-iodobenzoate.

Меглумина Амидотризоат

$C_{11}H_9I_3N_2O_4.C_7H_{17}NO_5$ = 809.1.

CAS — 131-49-7.

ATC — V08AA01.

ATC Vet — QV08AA01.

Description. Meglumine amidotrizoate contains about 47.1% of I.

Pharmacopoeias. In *US.*

USP 31 (Diatrizoate Meglumine). A white, odourless, powder. Freely soluble in water. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Sodium Amidotrizoate *(BANM, rINN)*

Amidotrizoate de Sodium; Amidotrizoato de sodio; Diatrizoate Sodium; Natrii amidotrizoas; Natrio amidotrizoatas; Natriumamidotritsoaatti; Natriumamidotrizoat; Nátrium-amidotrizoát; Natrium-amidotrizoát; NSC-61815; Sodium, amidotrizoate de; Sodium Diatrizoate; Sodu amidotrizoat. Sodium 3,5-diacetamido-2,4,6-tri-iodobenzoate.

Натрия Амидотризоат

$C_{11}H_8I_3N_2NaO_4$ = 635.9.

CAS — 737-31-5.

ATC — V08AA01.

ATC Vet — QV08AA01.

Description. Sodium amidotrizoate contains about 59.9% of I calculated on the anhydrous substance.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *US.*
Chin. includes the injection.

Ph. Eur. 6.2 (Sodium Amidotrizoate). A white or almost white powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in acetone. A 50% solution in water has a pH of 7.5 to 9.5. Protect from light.

USP 31 (Diatrizoate Sodium). A white, odourless, powder. Soluble in water; slightly soluble in alcohol; practically insoluble in acetone and in ether.

Incompatibility. Incompatibilities of sodium amidotrizoate with some antihistamines have been reported.

Adverse Effects and Treatment

Amidotrizoates and other iodinated contrast media may cause adverse effects due to direct toxicity, which tends to be dose-related and predictable, but use often leads to unpredictable or anaphylactoid reactions. Most reactions occur within 5 to 10 minutes and are mild and transient; however, severe, life-threatening reactions may also occur, and delayed reactions have been reported.

Direct toxic effects of iodinated contrast media are related to the osmolality of the solutions used and are most common with the amidotrizoates and other ionic monomeric compounds, which have a high osmolality. The route, the speed with which it is given, and the volume, concentration, and viscosity of the solution, also affect the incidence of adverse effects. For ionic media, the cation is also important: meglumine salts are generally better tolerated, but sodium salts have a lower viscosity and may produce fewer arrhythmias, and preparations containing a mixture of the salts are therefore often used. Anaphylactoid reactions are also more common with high-osmolality, ionic contrast media.