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SCIENTIFIC REVIEW

Adverse Reactions to Radiopharmaceuticals (ARRP): Particularly To Technetium Radiopharmaceuticals

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Summary

Radiopharmaceuticals are radioactive compounds that are prepared by a radiopharmasist and used in Nuclear Medicine departments for diagnostic or therapeutic purposes of human diseases. They are generally used i.v. so they have to be sterile and apyrogenic like other parenteral drugs. Effecting in a correct way and localising in the desired tissue with a sufficient amount, physicians and Nuclear Medicine staff have to be aware of the ***adverse reactions to radiopharmaceuticals (ARRP)*** *for the safety point of view. ARRPs are the clinical symptoms that are unexpected or unusual and undesirable. ARRPs are generally mild, reversible, not so much serious, and generally do not need any medical treatment. Reporting ARRPs by fulfilling the ARRP reporting and monitoring forms are critical for informing the physicians and the authorities about the problems about that radiopharmaceutical like drug interactions, altered biodistribution, wrong injection site or route and the in vivo stability of that radiopharmaceutical and by this way wrong diagnosing the disease may be prevented. But there are some defects in fulfilling the adverse reaction reporting forms in Turkey like the other countries.*

Key words: *Tc-99m radiopharmaceuticals, adverse reactions, iatrogenic reactions.*

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Radyofarmasötikler ile Görülen Advers Etkiler: Özellikle Teknesyum Radyoarmasötikleri ile Görülen Etkiler

Özet

Radyofarmasötikler, radyofarmasist tarafından hazırlanan ve insanlarda teşhis veya tedavi amacıyla Nükleer Tıp departmanında kullanılan radyoaktif ilaçlara denilir. Genel olarak i.v. olarak uygulanırlar bu nedenle diğer parenteral preaparatlar gibi steril ve apirojenik olmaları gerekir. Doktorlar ve diğer Nükleer tıp çalışanları, radyofarmasötiklerin düzgün bir şekilde etki göstermesi ve istenilen dokuda yeterli miktarda tutulmasını sağlamak için radyofarmasötiklerin advers etkilerinin (ARRP) farkında olmalı ve güvenli ilaç uygulanması açısından bu konuya dikkat etmelidirler. Advers etkiler, beklenmeyen veya sıklıkla olmayan ve istenilmeyen klinik septomlardır. Radyofarmasötiklerle görülen advers etkiler genellikle hafif, geçici, herhangi bir tıbbi müdahale gerektirmeyen ve çok ciddi olmayan reaksiyonlardır.

Radyofarmasötiklerde görülen advers etkilerin, ARRP bildirim ve izleme formlarının doldurulması suretiyle rapor edilmesi, Nükleer tıp uzmanlarını ve ilgili otoriteleri radyofarmasötiklerde görülen ilaç etkileşimleri, değişmiş biyodağılım, yanlış enjeksiyon yeri ve uygulama yolu ve in vivo stabilite gibi sorunlar hakkında bilgi sahibi yapacak ve bu şekilde hastalığın yanlış teşhis edilmesi olasılığını azaltmaya yardımcı olacaktır. Ancak Türkiye'de de diğer ülkelerde olduğu gibi radyofarmasötiklerde görülen advers etki bildirim formlarının doldurulması konusunda eksiklikler bulunmaktadır.

Anahtar kelimeler: *Tc-99m radyofarmasötikleri, advers etkiler, iatrojenik etkiler.*

INTRODUCTION

Definition of ARRP and Its Importance

An adverse drug reaction is any undesirable effect of a drug beyond its anticipated therapeutic effects occurring during its clinical usage. Radiopharmaceuticals are radioactive compounds that are used in Nuclear Medicine departments for the purpose of diagnosis generally and sometimes

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for the therapeutical purposes and are prepared by a qualified person like radiopharmasists. The adverse reactions to radiopharmaceuticals can rarely be seen when compared to use of conventional pharmaceutical drugs. The sterility and the apyrogenity are critical for the radiopharmaceuticals because of their administration in i.v route generally. Depending on the importance of safety, quality control tests of radiopharmaceuticals take a serious importance. In EU, they are considered as a special group of medicine that have been used for many years. Therefore, their preparation and use are regulated by EU directives, regulations and rules. These rules can be adopted by member states. Most of them are used for diagnostic purposes. They usually have no pharmacological effects and they were administered in very small amounts as microdoses. Because of this reason, the incidence of ***adverse reactions to radiopharmaceuticals (ARRPs)*** are generally minor and rare. However, therapeutic radiopharmaceuticals can cause tissue damage because of high radiation (1-3).

ARRP is any unexpected, unusual or undesirable effect of a drug beyond its anticipated therapeuic effects occuring during its clinical usage. The main reason of ARRP depends on the vehicle carrying the radiation, not the radiation itself. Radiation exposure should be justified by the expected diagnostic/ therapeutic benefit. In case of radionuclidic therapy, the injected activity should generate a minimal irradiation of non-targeted tissues such as non-tumoral tissues. It is important to notice the harm of radiation although the risk of radiation-induced cancerogenesis is lower than the pathology itself. ARRP can be classified as Type A or Type B reactions. **Type A reactions** are generally exaggerated but otherwise normal responses. They are generally dose-related, and reversible in the case of decreasing the dose or withdrawing the drug. They are common but rarely serious and might be increased by drug interactions. **Type B reactions** are mostly abnormal effects, unexpected and unpredictable from the known pharmacology of the drug. Type B reactions are not dose-related. They are rare but can be serious. Type A adverse drug reactions are more common than type B reactions and comprise 80% of all the adverse drug interactions. Adverse reactions generally include sensitivity reactions, many systematic and physiologic symptoms. Most common Type A adverse reactions are itching, nausea, coughing, bronchospasm, dyspne, flushing, chills, bradycardia, change in blood pressure, muscle cramps and dizziness. While some reactions happen immediately, some are formed in later times after administration (1,3,4).

Type B reactions are generally hypersensitivity reactions including anaphylaxis, serum sickness, cytotoxic reactions and delayed hypersensitivity reactions. Anaphylactoid reactions are immediate hypersensitivity reactions like urticaria, shock, and angio-derma. Generally initial sensitizing exposure is not found but anaflactoid life treatening reactions are probably due to histamine release with small molecule radiopharmaceuticals. These may act as haptens in association with native proteins. Histamine release can be formed with polyvinil propylene (PVP), dextran, poloxamers and murine radiolabeled antibodies that can be Mouse monoclonal antibodies (mAb) and chimeric Human Mouse Monoclonal Antibodies for radioscintigraphy. Dextrans are used for sedimentation aids during blood cell labeling procedures and poloxamers are used in kit preparations for ^{99m}Tc radiopharmaceuticals. Cytotoxic reactions are generally formed by the interaction of the antibody with the radiopharmaceutical hapten that is fixed to the cell membrane. Thus, this interaction causes complement activation. This complement activation, immune complex deposition in tissues and damage to the capillary endothelium can cause serum sickness type effects like skin reactions. Skin reactions can be formed within a very short exposure time and with a very small quantity of radiopharmaceuticals that develop within a few days. Delayed hypersensitivity type reactions are formed rarely with radiopharmaceuticals and that are generally T-cell mediated reactions like contact dermatitis (1, 5).

In USA, The American Society of Nuclear Medicine collects these adverse reaction reports depending on the administration of radiopharmaceuticals to patients. In Europe, these reports are collected by

The Joint Committee on Radiopharmaceuticals of the European Nuclear Medicine Society. The total incidence of ARRP in U.S is about 2.3 reactions per 100.000 administration. But, this rare incidence of adverse reactions is probably not accurate depending on the negligability in reporting them by physicians and Nuclear Medicine staff. No fatal case has been reported, the incidence of severe reactions is very low and minor due to the use of very small amount of radipharmaceuticals and better formulating and manufacturing procedures nowadays (1, 6, 7).

A similar small scale study was performed by the contribution of 17 nuclear medicine departments among Europe during 1996 for obtaining data on the prevalence of ARRP by the leading the Radiopharmacy Committee of EANM. After 10^5 administration, a prevalence of 11 events were recorded. There was no record about the fatality and severe side effect. This study was performed by modifying the study that was made in USA by Silberstein et al (6, 7). The slightly high incidence that was observed in Europe may be due to its small scale. The prevalence of ARRPs is approximately 1000-fold less than the adverse reactions that were observed depending on the administration of conventional pharmaceuticals and diagnostic contrast media (8).

According to the EANM annual report 2001, the incidence of ARRP is very rare and mostly of minor grades than conventional other drugs. The incidence of ARRP has been reported as 0.025% while it has been reported 0.7-1.5% for general drugs and 4-12.5% for X-ray contrast agents (1,9).

According to the EANM results, between 1993-1995 only three adverse reactions have been reported associated with the use of ^{99m}Tc-pyrophosphate, which is a bone scintigraphy agent. Two of them were vasomotor symptoms and minor, whereas, one of them was skin necrosis and severe (1).

UK Adverse Reaction Reporting Scheme has revealed that the pattern of ARRP incidence has dramatically changed due to the discontinuance of older radiopharmaceuticals, changes in quality control measures, and also to the introduction of methylene diphosphonate for bone imaging and colloids for reticulo-endothelial (liver) scans between 1977–1983 (9).

In New South Wales, while most of the majority of the maladministrations depend on the incorrect dispensing of radiopharmaceuticals (61%), incorrect reading of labels on the syringe (14%) and incorrect identification of patients (12%) are also other reasons that cause ARRPs. It has been reported that most of ARRPs are observed by application of ^{99m}Tc-based radiopharmaceuticals (84%) for diagnostic use and ^{131}I for therapeutic use. 96% of the cases are diagnostic radiopharmaceuticals and no immediate adverse effect has been seen. However, sometimes unwanted hypothyroidism can be developed depending on the maladministration of ^{131}I for therapy (10).

For the case of USA, the Radiological Society of North America (RSNA), Society of Nuclear Medicine (SNM) and the United States Pharmacopeia (USP) have carried out a collaborative study to obtain more accurate and descriptive information related with ARRPs. A study about the awareness of the ARRP was made on 3000 randomly selected physicians in a variety of specialty and the results showed that only 57% were aware of any adverse reaction reporting system. This incidence is not very promising because of the fact that this system was initiated about 20 years ago by FDA. Although 14% of these physicians had observed an adverse drug reaction in the previous year, only 5% of them had reported the following year (6, 7).

Another 4-year study was conducted in USA with the collaboration of 22 institutions for determining the prevalence of adverse reactions to both positron emitting radiopharmaceuticals and nonradioactive drugs used in interventional nuclear medicine during PET studies using questionnaire, which indicated for each month of the study the number of PET procedures performed, the number of adverse reactions to PET radiopharmaceuticals as well as the number of adverse reactions to interventional nonradioactive pharmaceuticals used for PET. No adverse reactions were reported related with any PET radiopharmaceutical dose. There were no

deaths or hospitalizations caused by nonradioactive interventional pharmaceuticals used adjunctive to PET studies. As a result, it can be claimed that PET radiopharmaceuticals are shown extraordinary safety but the failure in reporting system may depend on the physicians' being too busy. His wrong belief that the reaction is a not an adverse effect or because of the deficiency in achieving the reporting form in the hospitals might have misleading effects on evaluation of the data (11).

USP Drug Product Problem Reporting Program for Radiopharmaceuticals can be used both for reporting adverse reactions and for determining altered biodistribution of radiopharmaceuticals in USA. By these reports, the level of the probability of ARRP can be determined (6).

Commonly seen ARRPs in USA can be clasified as (6);

- Any adverse effects that are rare or frequent
- Adverse effects which are never seen nor reported
- Life-treatening or fatal reactions caused by the nonradioactive drug used for pharmacology, the sort of which may require hospitalization.
- Allergic or anaphylactoid reactions that are suspected or proved.
- Radiopharmaceuticals that are misadministered.

Not reported ARRPs in USA are (6);

- Bradycardia caused by hypotension
- Poor injection techniques that cause injuries.
- The effects that are due to the use of unsealed vials or sources. Ex; β-emitting therapeutical radiopharmaceuticals can cause cytopenia or ^{131}I can cause some neck pains.

Depending on various estimations ARRPs are 1-6 in 100.000 injections in all over the world, but this value may not really be accurate depending on the deficiency in filling out the ARRP forms by the Nuclear Medicine staff. But the adverse reactions that are formed depending on the administration of radiopharmaceuticals are generally mild because generally low volumes and microdoses are used.

In Turkey, ARRP shoud be reported to the Adverse Drug Reaction Monitoring Unit that is a part of the Turkish Ministry of Health, General Directorate of Drug and Pharmacy Affairs that is a part of the European organisation. So far, there have not been any feedback provided to the Turkish Ministry of Health, General Directorate of Drug and Pharmacy Affairs depending on the administrations of the radiopharmaceuticals (5, 12-14).

ARRP to Technetium Radiopharmaceuticals

As it is mentioned above, ARRPs are generally mild reactions depending on the use of the radiopharmaceuticals in low volumes and with low doses. They generally require little or no medical treatment and they are generally reversible. As generally known, radiopharmaceuticals consist of 2 parts, namely the radioactive part and the pharmaceutical part. ARRPs generally depend on the vehicles or the kit components that are used for the preparation of radiopharmaceuticals, not from the radioactive part. Especially for the diagnostic ones, the radiation dose is in a tracer dose, thus, almost no adverse reactions are formed. These incidences of ARRPs between 1957 and 2009 occur depending on the lung visualisation agent ^{99m}Tc-macroaggregated albumin (^{99m}Tc-MAA) (1 in 400 injection) and the bone-seeking radiopharmaceutical ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) (1 in 800 injection). Skeleton scanning agent diphosphonates are the most common radiopharmaceuticals that cause adverse effects. Erythema, nausea, vomiting and malaise are some of the typical diphosphonate reactions and may start after 2-3 hours of the injection. Respiratory or circulatory collapse and loss of consciousness are some of these adverse reactions. Additionaly, several fatalities have been reported with the liver scanning agent ^{99m}Tc-albumin colloid. The adverse reactions detected in clinical applications of colloids can be classified under the titles of vasomotor effects such as faintness, pallor, diaphoresis or hypotension and anaphylactoid effects (nausea, dermographism, wheezing, bronchospasm, erythema). Another radiopharmacutical group that causes adverse effects are liver and spleen scintigraphy agent colloids. Nausea, flush and pulse changes are some of the typical colloid reactions. ^{99m}Tc-sestamibi administrations may

also cause the development of anaphylactoid reactions. Additionally, ^{18}F-FDG may give false positive reactions. Disposition of the radiopharmaceutical can also be the reason of ARRP (3, 14, 15).

In USA among many different radiopharmaceuticals that are used in the Nuclear Medicine clinicals, ^{99m}Tc-albumin microspheres had the highest incidence of adverse reactions. ^{99m}Tc-sulphur colloid follows it in the second order. ^{99m}Tc-MAA, ^{99m}Tc-MDP, ^{99m}Tc-DISIDA are the other radiopharmaceuticals that cause adverse reactions frequently. Although most of them are very rare and need no special medical treatment, if needed, antihistamines or aminophylline can be a choice for the treatment of anaphylaxis. A similar situation is also true for France (1, 16).

Some ARRP examples about using ^{99m}Tc radiopharmaceuticals for systemic diagnostic purposes are (5, 8, 15);

Sodium Pertechnetate (Tc-99m); can cause allergic reactions like itching, skin rush, urticaria. They are very rare and can be cured.

Technetium (Tc-99m) Methylene Diphosphonate (MDP); Allergic reactions can be seen on performing a bone scan with Tc-99m MDP, and the most common adverse or allergic reaction is rash. In 1993 the most commonly used and documented ARRP was observed depending on the use of diphosphonate, MDP because of their common utilization for bone scanning in Nuclear Medicine procedure. The symptoms with the use of MDP are nausea, malaise, vertigo and pruritus.

Technetium (Tc-99m) Pyrophosphate; Allergic reactions can be rarely seen. They may need medical treatment. According to the results of EANM between 1980-2001, ^{99m}Tc-bone scanning phophates/phosphonates may be seen in 46 cases/157=30%.

Technetium (Tc-99m) (Pyro- and Trimeta-) Phosphates; Skin rush and itching can be seen and may need medical treatment.

Technetium (Tc-99m) Albumin; Rarely seen and mild. Although they usually do not need to be treated; therapy may be necessary if asthma or skin rush has developed. According to the results of EANM between 1980-2001, ^{99m}Tc-albumin particulates are 14 cases/157=29%. MAA (Lyomaa®, Pulmocis®) may cause chest pain, rigor, collapse and deaths with an incidence of 57%, microspheres may cause flush, pallor, rigor, nausea, sweat, dyspnea with an incidence of 36%, colloids (Nanocoll®) may cause cramps, nausea, dyspnea, hypotension with an incidence of 7%.

Technetium (Tc-99m) Albumin Aggregated; Tc-99m aggragates can cause hemodynamic and idiosyncratic reactions. While syanosis, rattle, neck stiffness, hardness in breathing can rarely be seen, redness of face, sweating, nausea can be formed very frequently. Medical treatment may be needed unless it is reversible.

Technetium (Tc-99m) Albumin Colloid; Allergic reactions such as cough, redness of face, skin rush, urticaria, distention at legs, arms, whezzy breathing can be developed. These are the initial symptoms of serious anaflactoid reactions and need medical intervention. Stomachache, vertigo, skin rash, sweating, nausea can be seen rarely. If not reversible may need medical treatment.

Technetium (Tc-99m) Sulphur Colloid; Rare cardiopulmoner arrest is reported. Allergic reactions, bronchospasm with or without oedema, fewer, hypotention, pain at the site of injection. Slow or unregular heartbeat can be seen and may need medical treatment. These may be initial symptoms of more serious anaflactoid reactions. Allergic reactions and fewer may be formed depending on the use of stabilizers like gelatin in the formulation. Medical treatment may be needed only in very rare effects.

Technetium (Tc-99m) Arcitumomab; Patients that use rodent based antibodies, can develop allergic reactions. Although no serious allergic reports are made during clinical experiments, medical attempt should be needed if these symptoms are in a manner of feeling discomfort.

Technetium (Tc-99m) Bicisate; Hardness in breathing,

hallucination, hypertension, angina, agitation or anxiety, vertigo, dizziness, sleepiness, nausea, parosomia may need treatment.

Technetium (Tc-99m) Gluceptate; Allergic reactions like skin rush, urticaria, itching can be seen rarely.

Technetium (Tc-99m) Lidofenin; Cold, skin rash, can be developed rarely and mostly does not need any treatment. But treatment can be needed in case of the continuous and repeated symptoms.

Technetium (Tc-99m) Mebrofenin; There are no known serious adverse effects.

Technetium (Tc-99m) Medronate; Some allergic reactions can be seen, which may need medical treatment.

Technetium (Tc-99m) Mertiatide; Allergic reactions, alteration in the blood pressure, epilepsy, tachycardia can be seen. If they become intensive, medical treatment may be needed.

Technetium (Tc-99m) Nofetumomab Merpertan; Mild and short lived allergic reactions can rarely be observed.

Technetium (Tc-99m) Oxidronate; Allergic rections, nausea and vomitting can rarely be observed and sometimes may need medical treatment.

Technetium (Tc-99m) Pentetate; Rare allergic reactions.

Technetium (Tc-99m) Sestamibi (MIBI); Cardiolite® is its commercial kit and is used in cardiac imaging. It is characterized with acute shortness of breath, itching, hypotension, bradicardia. Only one serious hypersensitivity case has been reported. Rash on body and extremities 2 days after injection can be seen. Metallical or bitter taste can be seen in the case of continuous and discomfortable it may need medical treatment.

Technetium (Tc-99m) Succcimer; Fewer, skin rash, stomachache, nausea and faint can rarely be seen and may need medical treatment.

Technetium (Tc-99m) Teboroxime; Pain in the site of injection, hypotension, metallical taste, nausea can rarely be seen.

Technetium (Tc-99m) Tetrofosmin; Rare allergic reactions like skin rush, breathing hardness, angina type chest pain, hypertension can be seen and may need medical treatment. Gastrointestinal symptoms, hypotention, vertigo, metallical taste and abnormal smelling may rarely be developed.

Technetium (Tc-99m) DTPA; Allergic reactions may occur; and in the case of intensiveness, medical treatment may be needed. According to the results of EANM between 1980-2001, ^{99m}Tc-DTPA (Technescan DTPA®, Pentacis ®) may be seen in 26 case/157=16.5% and depending on the use of furosemide vasomotor symptoms may occur with an incidence of 92%, hypotension with an incidence of 61%, nausea (27%), brochospazm (4%) and skin reactions (8%) may also be seen.

Technetium (Tc-99m) Betiatide (MAG-3): Technescan®is its commercial kit that is used for visualizing kidneys and their functions. Adverse reactions are rarely seen with its use in Nuclear Medicine Departments. Heavy eyes and feeling warm can be seen 20 min after injection.

According to the US results in 1997, adverse reactions to some of the radiopharmaceutical injections other than ^{99m}Tc-radiopharmaceuticals are given in (Table 1).

Iatrogenic Changes in the Biodistribution of Radiopharmaceuticals

Iatrogenic reactions are one of the very important form of ARRP. Both the interaction of the radiopharmaceuticals with other drugs that the patient use daily or at the time of the administration and the maladministration procedure of radiopharmaceuticals originating from the physician or the other hospital staff like nurses, therapists etc cause the formation of ***iatrogenic reactions***. The interaction of more than one drug in a therapeutical procedure may have a changing effect on the biodistribution. Generally patients may use several drugs at the same time depending

Table 1. ARRPs that are caused by using different ^{99m}Tc-radiopharmaceuticals commonly used in Nuclear Medicine Departments (8).

Radiopharmaceutical	Reaction	Classification
^{67}Ga-citrate	Stomach pain and melana 24 h after injection. Known hepatitis, anemia	Unlikely
^{131}I-NaI	Itching red 12 h after 1.85 MBq	Possible
^{131}I-NaI	Sore throat, tender at front of neck 48 h after 406 MBq	Probable
^{131}I-iodocholesterol (Norchol®)	Heat and pain at kidney level on injection	Possible
^{123}I-MIBG (Iobenguane)	Strange test and neusea on injection	Probable

on the therapy regime and the diagnostic protocol in Nuclear Medicine clinics. Iatrogenic reactions can be formed because of pharmacological action, in vivo interaction between the medication and radiopharmaceutical, drug-induced disease and interaction with catheters or syringes. The most serious ones are formed due to the use of cortisone or cytotoxic agents prior to tumour scintigraphy. Other important ones occur in patients that are used in iron preparations prior to bone scanning. Many drugs may alter hormonal status, thus, may cause serious changes in biodistribution. Gonadotrophins, digitalis, phenothiazines, diethylstilbestrol and cimetidine may enhance estrogen levels in high doses (11).

Several drugs may affect the biodistribution of radiopharmaceuticals, which is an important factor in the correct diagnosis of the desired area in scintigraphy. Altered biodistribution can be developed due to the secondary drug, which may be undesirable or on purpose. In most cases, patients can use different drugs that can interfere with its effect. Knowing the information on the undesired effect of interaction of the radiopharmaceutical with the other drugs may help the physicians to know the alteration of the biodistribution of that radiopharmaceutical, which may prevent them to diagnose in the wrong way. It may also cause an undesirable effect due to the less localisation of it in the target tissue or enhanced localization in the desired tissue/organ. Various imaging procedures and drugs that have effects on the biodistribution of radiopharmaceuticals are present and some of them are listed in Table 2 (1).

CONCLUSION

Adverse reactions are defined as noxious or unintended reactions to drug administered in standart dose through the proper route. Many adverse reactions related to radiopharmaceuticals used in nuclear medicine for diagnostic and therapeutic purposes are not reported due to failure in reporting system, which may be the result of the physician's being too busy or his wrong belief that the reaction is not an adverse effect or because of the deficiency in achieving the reporting form in the hospitals. On the other hand, collecting these data and providing the access by all nuclear medicine staff might be helpful to decrease the incidence of ARRPs and to prevent misdiagnosis. In this point, radiopharmasist can play a fairly important role and can help physicians in reporting and documenting ARRPs.

Table 2. The iatrogenic effects of some drugs in the biodistribution of some commanly used radiopharmaceuticals (1).

Imaging Procedure	Drug	Change in Biodistribution
^{99m}Tc-SC (for RES imaging)	Estrogens	Focal areas of decreased uptake in liver
	Al^{+3}, Mg^{+2}	Increased lung activity
	Anesthetics	Increased splenic uptake
	BCNU	Decreased splenic uptake
^{99m}Tc-phosphonate compounds (for bone imaging)	Chemotherapeutic agents	Increased renal activity
	Meperidine	Soft tissue uptake
	Corticosteroids	Decreased bone uptake
	Cytotoxic therapy	Increased uptake in calvarium
	Iron dextran	Increased uptake at injection site
	Melphalan	Increased bone uptake
	Dextrose	Increased renal activity
	Aluminum ion	Increased liver activity
	Iron	Increased renal activity
	Phospho-soda	Decreased bone uptake
^{99m}Tc-IDA derivatives (for hepatobiliary imaging)	Atropine	Prolonged gallbladder activity
	Cholecystokinin	Increased gallbladder contraction
	Nicotinic acid	Decreased hepatic uptake
	Narcotic analgesics	Prolonged liver-to-duedonum transit time
^{99m}Tc-labeling RBCs (in vivo labeling)	Penicillin	Poor labeling
	Dextran	Poor labeling
	Heparin	Poor labeling
	Doxorubicin	Poor labeling
	Iodinated contrast media	Poor labeling
	Hydralazin	Poor labeling
^{201}Tl chloride (for myocardial perfusion imaging)	Isoproterenol	Increased myocardial uptake
	Dipyridamole	Increased myocardial uptake
	Digitalis glycosides	Decreased myocardial uptake
	Propranolol	Decreased myocardial uptake
	Furosemide	Increased myocardial uptake
^{67}Ga-citrate (for tumor and inflammatory imaging)	Chemotherapeutic agents	Diffuse lung uptake
	Antibiotics	Uptake in colon and kidneys
	Estrogens	Uptake in mammary tissue
	Desferoxamine (before ^{67}Ga injection)	Decreased uptake
	Desferoxamine (after ^{67}Ga injection)	Increased uptake
	Iron dextran (before ^{67}Ga injection)	Decreased uptake
	Iron dextran (after ^{67}Ga injection)	Increased uptake
^{131}I-NaI (for thyroid uptake and imaging)	Iodide-containing preparations (Lugol's solution, SSKI, cough medicine etc.)	Decreased uptake
	Contrast media	Decreased uptake
	Natural or synthetic thyroid preparations (Synthroid, Cytomel)	Decreased uptake
	Antithyroid drugs (Propylthiouracil, Tapazole)	Decreased uptake
	TcO_4^-, Br^-, ClO_4^-, SCN^-	Decreased uptake

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