Prevalence of Adverse Reactions in Nuclear Medicine

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This investigation sought to determine the prevalence of adverse reactions to radiopharmaceuticals and to nonradioactive drugs used in interventional nuclear medicine. We also tabulated all adverse reactions reported to manufacturers of radiopharmaceuticals commercially available in the United States. **Methods:** A prospective 5-yr study was performed of 18 collaborating institutions using a questionnaire which enumerated monthly the number of procedures used and adverse reactions noted. An algorithm to determine the level of etiologic probability of an adverse reaction from an administered radiopharmaceutical was developed. We reviewed all available literature on adverse reactions in nuclear medicine. **Results:** During this period, 783,525 radiopharmaceutical and 67,835 nonradioactive drug administrations were analyzed. Ten of the 18 adverse reactions to radiopharmaceuticals were rashes. No patient experiencing an adverse reaction to a radiopharmaceutical required hospitalization or had significant sequelae. Reproducibility of the adverse reactions algorithm was validated by independent evaluation of 30 adverse reaction reports from the U.S. Pharmacopeia–Society of Nuclear Medicine adverse reaction reporting system. All adverse reactions to 49 commercially available radiopharmaceuticals were tabulated and referenced. **Conclusion:** Radiopharmaceuticals have an excellent safety record. An algorithm to evaluate putative radiopharmaceutical reactions is highly reproducible.

Key Words: adverse reactions; radiopharmaceuticals

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Unlike drugs given for therapeutic purposes, radiopharmaceuticals rarely cause adverse reactions. The explanation for the safety of radiopharmaceuticals lies not only in the very small mass of drug injected or ingested, usually in the microgram range, but also because radiopharmaceuticals are typically administered only once or a very limited number of times to any given patient. The use of a radiopharmaceutical is not based upon its ability to produce a pharmacological effect, but rather on differences in the distribution and pharmacokinetics of the agent between normal and abnormal physiological processes. In fact, the production of pharmacological or physiological effects by a radiopharmaceutical is undesirable since the agent should not modify the parameter it is attempting to measure. Unusual ("idiosyncratic") sensitivity to a pharmacologic effect is virtually never seen.

Estimates of adverse reaction prevalence are difficult to assess, partly because of physician ignorance of available reporting schemes. In a recent study of 3000 randomly selected physicians, only 57% were aware of any adverse reaction reporting system. Whereas 14% of the total had observed an adverse drug reaction in the prior year, only 21, or 0.7% of the total, had reported the occurrence. There are many reasons for not filling out adverse reaction reporting forms. Physicians may be too busy, be concerned about the time required, not have the form readily available, be anxious about potential liability or believe that the reaction is common knowledge (*1*). A reaction may also be missed if the patient leaves the nuclear medicine service before its occurrence (*2*). Confusion may also exist over the basic definition of adverse reaction. For example, the definition used by the Food and Drug Administration (FDA) for adverse drug experiences precludes any consideration of causality and includes types of adverse reactions not relevant to radiopharmaceuticals.

The current reporting system for adverse reactions in nuclear medicine has evolved over two decades in collaboration with the United States Pharmacopeia (USP) and FDA (*3–5*). Since 1986, the U.S.P. Drug Product Problem Reporting Program has provided, in cooperation with the Society of Nuclear Medicine (SNM), a form to be used for reporting both adverse reactions and altered radiopharmaceutical biodistribution. A copy of each completed report is sent to the FDA.

The prevalence of adverse reactions for radiopharmaceuticals, based on a variety of reporting systems and assumptions, has been estimated to range between 0.3 and $33/10^5$ administrations (*3,4,6–9*). For comparison, the reaction frequency to radiographic contrast media ranges between 3.8%–12.7% ($3.8–12.7/10^2$) for ionic contrast and 0.6%–3.1% ($0.6–3.1/10^2$) for nonionic contrast (*10–13*). Adverse drug reactions for all administered drugs in the hospital setting have been measured at 0.7%–1.5% or higher (*14,15*).

Estimation of the true frequency of adverse reactions is difficult not only because of reporting problems but also because the exact total number of doses administered is unknown. To obtain a more realistic estimate of the frequency of adverse reactions to radiopharmaceuticals, the SNM's Pharmacopeia Committee undertook a 5-yr prospective study of the prevalence of adverse reactions to radiopharmaceuticals and interventional drugs used in nuclear medicine beginning in September 1989.

MATERIALS AND METHODS

By consensus, the Pharmacopeia Committee established the following operational definition for an adverse reaction:

1. The reaction is a noxious and unintended clinical manifestation (symptoms, signs, laboratory data abnormalities) following the administration of a radiopharmaceutical or nonradioactive adjunct pharmaceutical.
2. The reaction is unanticipated from the known pharmacologic action of the nonradioactive pharmaceutical.
3. The reaction is not the result of an overdose (which is a misadministration).
4. The reaction is not the result of injury caused by poor injection technique.
5. The reaction is not caused by a vasovagal response (slow pulse and low blood pressure).
6. The reaction is not caused by deterministic effects of radiopharmaceuticals intended for therapeutic uses.
7. The definition excludes altered biodistribution which causes no symptoms, signs or laboratory abnormalities.

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Significant adverse reactions to be reported included:

1. Untoward effects whether previously reported frequently or rarely.
2. Untoward effects never before seen or reported following administration of the radiopharmaceutical.
3. Only life-threatening (i.e., requiring hospitalization) or fatal reactions from nonradioactive drugs (i.e., drugs used for pharmacologic intervention).
4. Reactions unanticipated from the known pharmacologic action of a nonradioactive interventional drug.
5. Anaphylactoid or allergic reactions.

Reactions not to be reported included:

1. Overdosages (misadministration).
2. Vasovagal responses (reported in European registries).
3. Injury from poor injection technique.
4. Deterministic effects from therapy with unsealed sources (e.g., myelosuppression from a therapeutic agent).

The Pharmacopeia Committee also addressed the problem of causality, the likelihood that an administered radiopharmaceutical causes an observed subsequent adverse reaction, by devising an algorithm which attempted to define the likelihood of an administered radiopharmaceutical leading to an observed adverse effect. Previous efforts devised for this purpose have been fraught with multiple problems:

1. It is difficult to be absolutely and unequivocally certain that an adverse reaction is or is not related to an injected radiopharmaceutical because there is always an underlying disease for which the test has been ordered.
2. The reaction rate is extremely low, so there is no vast experience with specific adverse reactions to radiopharmaceuticals being reported.
3. Literature references to radiopharmaceuticals are commonly based on case reports with no proof of causality.
4. The clinical and laboratory features of most reactions to radiopharmaceuticals are not unique.
5. Every radiopharmaceutical experience involves dechallenge or discontinuation of the drug following a single dose.
6. Rechallenge may not reproduce the adverse event, is not always feasible and, under some circumstances, could be unethical.

Algorithm

The following algorithm is suggested to categorize probabilities of causation.

Not Related. This category is applicable to those adverse experiences which, after careful medical consideration, are judged to be not related to the test material. Neither painful local sensation from drug infiltration nor hematoma at the injection site is an adverse reaction. An adverse experience may be considered causally *not related* if or when:

1. Only a vasovagal response to a radiopharmaceutical is documented (hypotension and slow pulse).

or, any three of the following are found:

2. It does not follow a reasonable time sequence from administration of the test material.
3. It could readily have been produced by the patient's clinical state, environmental effects or toxic factors of other materials administered to the patient.
4. It does not follow a known response pattern to the suspected test material.
5. It does not reappear or worsen if the test material is readministered.

Conditional, Unlikely or Remote. This category applies to those adverse experiences which, after careful medical consideration, cannot be placed in either "possibly related" or "not related" categories. This definition is to be used when exclusion of drug causality of a clinical event seems plausible but the precise criteria in the "not related" category cannot be met. It can represent the first reported true side effect of a radiopharmaceutical, but since it has never been reported before it would be registered in this category and would be moved to the "probable" list at a later time if more reports of the same reaction occurred. An adverse experience may be considered causally *conditional, remote or unlikely* if or when:

1. It follows a reasonable time sequence but does *not* follow a known response pattern to the test material administered.
2. It does *not* follow a reasonable time sequence from administration of the test material but does follow a known response pattern to the suspected test material.

Possible (Must Have All Three of the Following Criteria). This category applies to those adverse experiences for which, after careful medical consideration, the causality of the adverse reaction by the radiopharmaceutical appears possible if or when:

1. It follows a reasonable time sequence from administration of the test material.
2. It follows a known response pattern to the suspected test material.
3. It could also have been produced by the patient's clinical state, environmental or toxic factors, other diagnostic or therapeutic interventions, including other medications, contrast media, etc. administered to the patient.

Probable (Must Have First Two Plus Numbers 3 or 4). This category applies to these adverse experiences which, after careful medical consideration, are thought, with a high degree of certainty, to be related to the test material. Causality of an adverse experience may be considered probable if or when:

1. It follows a reasonable time sequence from administration of the test material.
2. It follows a known pattern of response to the suspected test material.
3. It could not be reasonably explained *solely* by the known characteristics of the patient's clinical state, environmental or toxic factors or other medications, contrast media, etc. administered to the patient.
4. If rechallenge is medically necessary, the reaction recurs.

We independently rated 30 case reports from the SNM Reporting Program for the level of causality to test the reproducibility of this algorithm.

Participating Institutions

On a prospective basis, a total of 18 institutions (Appendix A) that perform a high volume of nuclear medicine procedures completed and returned a form (Appendix B) indicating the number of radiopharmaceuticals and interventional pharmacologic administrations each month. Reported adverse reactions to specific radiopharmaceuticals by these institutions were investigated using the categories for causation described above. All reactions we have listed fulfilled the criteria for "possible" or "probable" adverse reactions.

In addition, we tabulated all adverse reactions reported for each radiotracer commercially available in the United States in 1995 in a matrix format which references all reported reactions. We were unable to classify the degree of association of these tabulated reported reactions with the allegedly causative radiotracer because there was not always enough clinical information.

TABLE 1
Adverse Reactions to 783,525 Radiopharmaceutical Dosages in the Study Population 1989–1994

Radiopharmaceutical	Adverse reaction	Number of cases
[^{67}Ga]gallium citrate	Rash	1
[^{131}I]iobenguane (MIBG)	Chest discomfort, light headedness	1
^{99m}Tc-macroaggregated albumin (MAA)	Rash	1
^{99m}Tc-medronate (MDP)	Rash	2
	Nausea	1
	Mild anaphylaxis	1
^{99m}Tc-oxidronate (HDP)	Rash	4
	Diaphoresis	1
^{99m}Tc-pentetate (DTPA)	Rash	1
^{99m}Tc-sestamibi	Rash	1
Stannous pyrophosphate (nonradioactive)*	Mild anaphylaxis	2
	Light headedness	1
^{99m}Tc-sulfur colloid	Nausea, vomiting, rash, headache	1
Total		18

*Administered intravenously to permit in vivo radiolabeling of erythrocytes and considered part of the final radiopharmaceutical.

RESULTS

We found 100% agreement on the classifications of the 30 cases analyzed from the SNM-U.S.P. Drug Problem Reporting Program using the described algorithm. Table 1 summarized 18 adverse reactions to radiopharmaceuticals in the "possible" or "probable" categories based on 783,525 injections. None of these was severe enough to cause hospitalization. The 95% confidence limits for the prevalence of such reactions is 1.2–3.4 per 100,000 injections. For interventional drugs, we recorded only adverse reactions leading to hospitalization (Table 2). There were no deaths. The 95% confidence limits for these reactions are 0.1–11.7 per 100,000 injections. Table 3 lists the prevalence of adverse reactions to both radiopharmaceuticals and nonradioactive pharmaceuticals appear. None of these was severe. In no case was hospitalization required and there were no sequelae.

Table 4 lists all referenced adverse reactions to commercially available radiopharmaceuticals.

DISCUSSION

The FDA uses the term adverse drug experience rather than adverse reaction and defines this as "any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: an adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose, whether accidental or intentional; an adverse event occurring from drug withdrawal; and any significant failure of expected pharmacologic action" (*16*). Radiopharmaceutical manufacturers are bound by this definition. It precludes, however, any consideration of causality and includes types of reactions not relevant to nuclear medicine. It was for these reasons that we developed a definition for adverse reactions that permits one to obtain a true estimate of the frequency of patient adverse reactions to radiopharmaceuticals.

TABLE 2
Severe Adverse Reactions to 67,835 Doses of Nonradioactive Pharmaceuticals Used in Nuclear Medicine

Drug	Reaction	Number of cases
Dipyridamole	Prolonged chest pain	2
	Syncope	1
Glucagon	Moderate anaphylaxis	1
Total		4

TABLE 3
Prevalence of Adverse Reactions in Nuclear Medicine

	Total adverse reactions	Total dosages	Prevalence	95% confidence limits
Radiopharmaceuticals	18	773,525	$2.3/10^5$	$1.2–3.4/10^5$
Nonradioactive drugs	4	67,835	$5.9/10^5$	$0.1–11.7/10^5$

Use of the prospective study approach with the 18 collaborating institutions guaranteed a reliable numerator and denominator for the frequency of adverse reactions. Our results (Table 3) are in the lower range of previous reported estimates. None of the observed reactions to radiopharmaceuticals were severe, requiring or prolonging hospitalization. There were no sequelae of any adverse reactions. Adverse reactions to radiopharmaceuticals are quite uncommon, occurring with a prevalence of $2.3/10^5$ in our study (0.0023%). Interventional pharmaceuticals (not tracers) used in nuclear medicine were also quite safe, with the risk of hospitalization following administration to be only of $5.9/10^5$. No lethal reactions occurred.

Moreover, we agreed on the classification of all 30 adverse reaction reports from the Society of Nuclear Medicine-U.S.P. Drug Problem Reporting Program, which further validates our algorithm.

The radiopharmaceuticals most commonly linked to adverse reactions over the past decade include ^{99m}Tc-sulfur colloid, ^{99m}Tc-methylene and hydroxymethylene diphosphonates (bisphosphonates) and ^{99m}Tc-human albumin microspheres, which is no longer produced. Any adverse event not previously described must be registered if there is even a remote chance of a causal relationship. The probability of causation between radiopharmaceuticals and effect will increase as more examples of the reaction are reported.

CONCLUSION

A prospective 5-yr study of the incidence of adverse reactions to radiopharmaceuticals and nonradioactive drugs used as adjuncts in nuclear medicine procedures was conducted by the SNM Pharmacopeia Committee. The total number of radiopharmaceutical and adjunct nonradioactive drug injections during this time period were 783,525 and 67,835, respectively. The total number of adverse reactions for radiopharmaceuticals and adjunct nonradioactive drugs were 18 and 4, respectively. The incidence rate for adverse reactions for radiopharmaceuticals and adjunct nonradioactive drug injections were 0.0023% and 0.0059%, respectively. These incident rates are 1000 times lower than that reported for x-ray contrast media and for drugs administered in a hospital setting.

Ten of the 18 adverse reactions reported in this study were rashes. None of the patients exhibiting an adverse reaction to a radiopharmaceutical required hospitalization; nor did any patient exhibit any lasting symptoms or sequelae. Interventional

TABLE 4
Reported Adverse Reactions to Radiopharmaceuticals Used in the U.S.*

	Chills	Fever	Nausea	Vomiting	Erythema, flushing	Diffuse rash	Pruritus	Hives/urticaria	Cardiac arrest	Chest pain, tightness or heaviness	Hypertension	Hypotension	Respiratory reaction	Tachycardia	Bradycardia	Seizures	Syncope or faintness	Dizziness, vertigo	Headache	Diaphoresis	Cyanosis	Anaphylaxis	Facial swelling	Abdominal pain	Arthralgia	Metallic taste	Asthenia	Pain/burning at inj. site	None	Comments, other reactions
^{57}Co-cyanocobalamin																													28	
Rubratope-57																													29	
Dicopac kit																														
[^{51}Cr]sodium chromate																													28	
Chromitope					29						29			29						29										
[^{18}F]fluorodeoxyglucose (FDG)																													28	
[^{59}Fe]ferrous citrate																													28	
																													29	
[^{67}Ga]-gallium citrate			28	28	18	16	16	16					18*	18			18	18				18			18**					*Dyspnea;** salty taste
Neoscan			29	29		27	27	28						28				27												
						28	28	29						29																
						29	29																							
[^{111}In]indium oxyquinoline		28				28	28	28																						
Oxine		29				29	29	29																						
^{111}In-pentetate (DTPA)		28	28	28	24		24	24	29*		24								28†											†Aseptic meningitis;
MPI-DTPA		29	29	29															29											*One death 20 min postinjection
^{111}In-pentetreotide, Octreoscan		29	29		29							29			29			29	29	29				29		29				One case of anemia
^{111}In-Satumomab pendetide																														28-confusion, diarrhea,
OncoScint CR/OV	28	28	28		18	28	28			28	28	28						28	28	28				28		28				*tachypnea
[^{123}I]iobenguane metaiodobenzylguanidine, (MIBG)			16		18						28		27*				16	27												
			27														27													
[^{123}I]iodohippurate sodium																														
¶Nephroflow, Nephropure			28	28		28	28	28				28																		
[^{123}I]iofetamine (I-d, I-N-isopropyl-p-iodoamphetamine hydrochloride, IMP) Spectamine			7			7				28	28							28												
[^{123}I]sodium iodide			16	28		28	28	28		28			16*	28			16		28											*tachypnea; 2-parosmia
			28	29		29	29	29		29				29																
			29																											

TABLE 4 (Continued)

	Chills	Fever	Nausea	Vomiting	Erythema, flushing	Diffuse rash	Pruritus	Hives/urticaria	Cardiac arrest	Chest pain, tightness or heaviness	Hypertension	Hypotension	Respiratory reaction	Tachycardia	Bradycardia	Seizures	Syncope or faintness	Dizziness, vertigo	Headache	Diaphoresis	Cyanosis	Anaphylaxis	Facial swelling	Abdominal pain	Arthralgia	Metallic taste	Asthenia	Pain/burning at inj. site	None	Comments, other reactions
[^{125}I]iodinated albumin (IHSA iodinated human serum albumin)						29																								
[^{125}I]sodium iothalamate Glofil																												29		
[^{131}I]iobenguane (MIBG)					27															27					25				27-tingling of arms and face	
[^{131}I]iodinated albumin (RISA, radioiodinated serum albumin) Megatope																												28		
[^{131}I]iodohippurate sodium			28	28			25	18				7	25*	7			7			18		18	18						*Dyspnea; †"cold sweat", pallor; amaurosis fugax	
Hipputope, Hippuran			29	29								28					18†					24							
												29																		
[^{131}I]sodium iodide	18		28	28		24	24	24		24				24				18	18											
Iodotope			29	29			28	28		28				28					28											
							29	29		29				29																
^{131}I-6-beta iodomethyl-18-norcholesterol			27	18	7					7	18	7	28*	23				7	18	27			18	18		18			27—frozen tongue; *dyspnea	
			28		18					28		23		27				28												
NP-59												28																		
^{81m}Kr																												28		
^{13}N-ammonia																												28		
[^{32}P]chromic phosphate suspension	28	28	28	28						28			28*											28						*Dyspnea, sore throat, cough, pleuritis
Phosphocol			29																					29						28-myelosuppression
^{32}P-sodium phosphate																												28		
^{82}Rb																														
^{89}Sr-Strontium chloride	28	28																												28-myelosuppression
Metastron	29	29																												Injectate also contained MDP and soluble albumin*
^{99m}Tc-albumin colloid	25		19		16	27	27				27	19	19	25				27		16		19*		19*						Tachypnea*, malaise
Microlite	27		27									27	27+	27										27						*Dyspnea
^{99m}Tc-albumin (HSA, human serum albumin)	18	18			18	28						18	28*	18				18					18							*Dyspnea
^{99m}Tc-antimony trisulfide colloid					27				19			19	19*	19					19		19									

TABLE 4 (Continued)

	Chills	Fever	Nausea	Vomiting	Erythema, flushing	Diffuse rash	Pruritus	Hives/urticaria	Cardiac arrest	Chest pain, tightness or heaviness	Hypertension	Hypotension	Respiratory reaction	Tachycardia	Bradycardia	Seizures	Syncope or faintness	Dizziness, vertigo	Headache	Diaphoresis	Cyanosis	Anaphylaxis	Facial swelling	Abdominal pain	Arthralgia	Metallic taste	Asthenia	Pain/burning at inj. site	None	Comments, other reactions
Lymph-scan ^{99m}Tc-bicisate dihydrochloride (ECD ethyl cysteinate dimer ECD) Neurolite			29			29				29			29*			29	29	29	29		29						29			Neurologic adverse events may have been related to underlying disease, including hallucinations, parosmia, also cardiac failure; *respiratory arrest
^{99m}Tc-disofenin Hepatolite																												16	
^{99m}Tc-exametazime hexamethylpropylene amine oxime (HMPAO) Ceretec		28 29	29		16	28 29					28 29	22	16*			25†				29	25	22	28 29	16						*Dyspnea †with myoclonus (labeled WBC)
^{99m}Tc-gluceptate Glucoscan, Techne-scan Gluceptate	24		18		18	28 29		28 29					18*	18		18		18	16	18										*Dyspnea
^{99m}Tc-lidofenin Techne-scan HIDA	28		28																										
^{99m}Tc-macroaggregated albumin (MAA)	17		28		18	18	24	17	18	28	17	18	24	17			18			28	28	25				24				*Dyspnea; throat tightness; 16-arm numbness; 17-parosmia
¶AN-MAA, Macrotec, MPI-MAA, Pulmolite, Techne-scan MAA	19				24 28		29	24 27	24	29	18	28	28*	18																
^{99m}Tc-mebrofenin Choletec								28 29																						
^{99m}Tc-medronate (MDP or methylene diphosphonate) Osteolite, Techne-scan MDP, AN-MDP, MPI-MDP	16 28 29	16 28 29	16 27 28 29	16 27 28 29	18 21 27	16 21 27 28 29	2 16 21 27	17 21 27 28 29	28 29*	16 17 27	27	27 28 29	16 18	27		27	16 27	2 16 18 29	16 18 19 27	16		18		16 27		27	17 18	27		27-photophobia; *one death secondary to cardiac arrhythmia
^{99m}Tc-mertiatide (MAG3, mercaptoacetyl-glycylglycylglycine) Techne-scan MAG3			25	25		16											27													27-sore, thick throat
^{99m}Tc-oxidronate (HDP, hydroxymethylene			7	28	28	7	27			27*							25			25			27							*Heart burn

TABLE 4 (Continued)

	Chills	Fever	Nausea	Vomiting	Erythema, flushing	Diffuse rash	Pruritus	Hives/urticaria	Cardiac arrest	Chest pain, tightness or heaviness	Hypertension	Hypotension	Respiratory reaction	Tachycardia	Bradycardia	Seizures	Syncope or faintness	Dizziness, vertigo	Headache	Diaphoresis	Cyanosis	Anaphylaxis	Facial swelling	Abdominal pain	Arthralgia	Metallic taste	Asthenia	Pain/burning at inj. site	None	Comments, other reactions
diphosphonate)			27			29														27										
Osteoscan-HDP			28																											
^{99m}Tc-pentetate	18		2		27	27	27	20			18	2	2	18			2		18		20	25			7			7		*Cough; †wheezing;
(DTPA, diethylenetri-	27		19			28	28	28				7	19*				18		27			26								trisodium salt can
aminepentaacetic acid)						29	29	29				19	20																	cause neurologic
Techne-scan DTPA, AN												20	27†																	signs if given
DTPA, MPI-DTPA,												27																		intrathecally
Techniplex																														
^{99m}Tc-pyrophosphate¶ (PYP)																														*Also from
Pyrolite, Techne-scan	18*	18*	18*	29	18*	16	18*	27		18*		18*	18*				27	18*							18*			27		nonradioactive PYP
PYP, Phosphotec, MPI-	28	28	28		27	18*	27					28						29												reagent kits; 4-tinnitus
Pyrophosphate, AN	29	29	29		28	27	29					29																		
Pyrotec, Ultratag					29	29																								
^{99m}Tc-sestamibi			16		28	27	27									28			16						27					27-tingling
Cardiolite					29	28										29			27						28					
						29													28						29					
																			29											
^{99m}Tc-sodium pertechnetate	27		18	18		18	18	29		18	18							14	18	14		29								
Minitec, UltratecKow			27			27																								
^{99m}Tc-succimer (DMSA,		29	28		28	29											28						28							
dimercaptosuccinic acid)																														
MPI-DMSA, Nephroscint			29		29												29						29							
^{99m}Tc-sulfur colloid																														*Wheezing, dyspnea,
AN-Sulfur Colloid,	18	28	16	28	29	27	16	28	29	28	29	28	28*	18	28	27	18	28	18	18	18	18			18			28		choking; 27–sneezing,
TechneColl, TcSC,		29	28	29		28	28	29				29	29			28		29				28						29		itchy throat; 17–
Tesuloid			29			29	29									29						29								paresthesia, weakness
^{99m}Tc-teboroxime			28									28											28			28		28		27–hand, arm
CardioTec																														numbness
[^{201}Tl]thallous chloride		16			16*	2	27					28																		*Erythema possibly
					18	27	28					29																		due to dipyridamole
					27	28	29																							
						29																								
^{127}Xe																												28		
^{133}Xe																												28		

* The radiopharmaceutical appears first. Chemical names are in parentheses. Commercial or trade names of the radiopharmaceutical appear last.
¶Numbers in table are either reference sources or letters to the author.

pharmaceuticals used as an adjunct to the nuclear medicine procedure can rarely lead to temporary hospitalization but at a prevalence of about 6 per 100,000 injections. None of these patients exhibited any sequelae.

APPENDIX A

Collaborating Institutions

University of Alabama, Birmingham, AL; M.D. Anderson Cancer Center, Houston, TX; University Hospitals of Cleveland, Cleveland, OH; Cornell Medical Center, New York, NY; Dana Farber Cancer Center, Boston, MA; Duke University Medical Center, Durham, NC; Cross Cancer Center, Edmonton, Alberta; Indiana University, Indianapolis, IN; University of Iowa, Iowa City, IA; University of Kentucky, Lexington, KY; Mallinckrodt Institute of Radiology, St. Louis, MO; Marshfield Clinic, Marshfield, WI; Massachusetts General Hospital, Boston, MA; Mayo Clinic, Rochester, MN; State University of New York, Syracuse, NY; Temple University Hospital, Philadelphia, PA; Univerity of Utah, Salt Lake City, UT; and Department of Veterans Affairs Hospital, Bay Pines, FL.

APPENDIX B

Monthly Radiopharmaceutical and Adverse Reaction Reporting Form

Society of Nuclear Medicine
Pharmacopeia Committee

1. _____ (Institution) _____ (Month) _____ (Year)
2. Total radiopharmaceutical doses for month (include IND, NDA and all other radioactive drugs and biologics for diagnosis and therapy) _____
3. Adverse reactions to radiopharmaceuticals:
   Yes _____ No _____ Date _____
   (If yes, describe with attached copy of U.S.P. Drug Product Problem Reporting Program form, which details the radiopharmaceutical, dose, route, reaction, etc.).
4. Total nonradioactive pharmaceutical doses for month used for procedures (include dipyridamole, adenosine, etc.) _____
5. Total nonradioactive pharmaceutical reactions causing hospitalization or death _____
6. Person completing form
   _____ (Please Print) _____ (Phone) _____ (Date)

Definition of Adverse Reaction

Patient adverse drug reaction is any response to a drug which is noxious and unintended, occurring at doses used in man for prophylaxis, diagnosis, therapy of disease, or for modification of physiological function.

Significant adverse drug reactions which should be reported include:

1. Untoward effects whether observed frequently or rarely.
2. Untoward effects never before seen following administration of the radiopharmaceutical.
3. Only life-threatening (requiring hospitalization) or fatal reactions from nonradiopharmaceuticals (i.e., interventional drugs).
4. Reactions unanticipated from the known pharmacologic action of a nonradioactive pharmaceutical.
5. Anaphylactoid or allergic reactions.

Do not report reactions from:

1. Overdose (this is a misadministration).
2. Vasovagal response.
3. Injury from poor injection technique.
4. Deterministic effects from therapy with unsealed sources (e.g., myelosuppression from a therapeutic agent).

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