

## Adverse Reactions to Contrast Media

A Report from the Committee on Safety of Contrast Media of the International Society of Radiology<sup>1</sup>

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**More than 300,000 case reports have been collected in a prospective survey of adverse reactions to intravascular contrast media. The reports were provided by radiologists in the United States, Canada, Europe, and Australia and represent the largest survey of its type to date. The overall incidence of reactions was about 5%, lower than any rate reported in the recent literature, and was strikingly similar in all participating countries.**

INDEX TERMS: Angiocardiography, contrast media • Angiography, contrast media • Aortography, contrast media • Cerebral angiography, contrast media • Cholangiography, contrast media • Contrast media, complications (Heart and great vessels, adverse reaction to contrast material, 5[0].448; Skull, adverse reaction to contrast material, 1[0].448; Vascular system, adverse reaction to contrast material, 9[0].448) • Contrast media, toxicity • Urography, contrast media • Venography, contrast media

Radiology 137:299-302, November 1980

**U**NDER the aegis of the Committee on Safety of Contrast Media of the International Society of Radiology, a total of 302,083 case reports have been collected in a prospective survey of adverse reactions to intravascular contrast media. This has been accomplished through the combined efforts of radiologists in the United States, Australia, Belgium, Canada, Norway, Sweden, and Yugoslavia. The largest contribution came from the United States and Canada as one unit, and the second largest from Italy. Contributions from other countries came in increments of 2,000-5,000 and were readily incorporated in the "major" United States pool. Many of our colleagues participated throughout the period of the survey, while several others contributed for only one or two years. However, each participant adhered faithfully to our protocol, which involved completing a report on every patient regardless of whether or not he experienced an adverse reaction, so that the incidence of reactions could be readily determined. (Some well-intentioned colleagues contributed interesting case reports in a rather irregular or haphazard manner. Their contribution and desire to help was acknowledged with great appreciation, but the data were not included in this study.) The form of the report was the same as that reported previously (6).

All reports were processed by W.H.S. except for the Italian forms which were processed by G.T. to eliminate the cost and difficulty of shipping more than 100,000 reports from Italy to the United States. Both the U.S. and Italian studies were conducted simultaneously using essentially the same computer program; this proved to be fortunate, as the two surveys gave similar results and thereby complemented and fortified each other. Each report was individually reviewed, classified, and processed and the data obtained were tabulated and analyzed.

TABLE I: INCIDENCE OF REACTIONS TO INTRAVASCULAR CONTRAST MEDIA

	No. of Patients Examined	No. of Patients with Reactions	Incidence of Reactions
Shehadi series	201,344	9,332	4.63%
Toniolo series	100,739	4,969	4.93%
Total	302,083	14,301	4.73%

### RESULTS

The data obtained to date, based on the 302,083 valid case reports, confirm the results and conclusions previously reported on behalf of the Committee (5). A comparison of the data from the two surveys (designated as Shehadi and Toniolo series) is presented in TABLES I-VI. Slight variations may be explained by differences in the number of cases reported for a given area of study, procedure, or type of examination. The slight difference in overall incidence between the Toniolo (4.93%) and Shehadi series (4.63%) should not distract the reader from the close similarities noted throughout.

#### *Incidence and Distribution of Reactions*

**Nonfatal Reactions:** The overall incidence of reactions (TABLE I) was lower than that reported in the recent literature, which was 8.5% for Ansel (1), 8.53% for Ochsner *et al.* (4), and 7% for Witten *et al.* (7). The rate was twice as high for excretory urography as it was for the arterial procedures, and approximately twice as high for intravenous cholangiography as it was for urography, making cholangiography the highest of all procedures. While the Toniolo series demonstrated 1% fewer reactions than the

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TABLE II: INCIDENCE OF REACTIONS TO INTRAVASCULAR EXAMINATIONS ACCORDING TO PROCEDURE

Procedure	Series	No. of Patients Examined	No. of Patients with Reactions	No. of Fatal Reactions	Incidence of Reactions
Urography	Shehadi	146,904	7,489	9	5.10%
	Toniolo	67,129	2,768	2	4.13%
	Total	214,033	10,257	11	4.80%
Cholangiography	Shehadi	6,628	693	2	10.46%
	Toniolo	27,150	1,983	0	7.32%
	Total	33,778	2,676	2	8.00%
Cerebral angiography	Shehadi	11,726	231	1	2.00%
	Toniolo	1,045	32	0	3.07%
	Total	12,771	263	1	2.06%
Angiocardiography	Shehadi	7,239	145	2	2.01%
	Toniolo	672	34	0	5.06%
	Total	7,911	179	2	2.26%
Aortography	Shehadi	21,506	552	0	2.56%
	Toniolo	3,379	113	1	3.34%
	Total	24,885	665	1	2.67%
Other arteriography	Shehadi	2,460	81	0	3.29%
	Toniolo	355	20	0	5.74%
	Total	2,815	101	0	3.58%
Venography	Shehadi	4,881	141	1	2.89%
	Toniolo	1,009	19	0	1.88%
	Total	5,890	160	1	2.72%

TABLE III: SEVERITY OF REACTIONS TO INTRAVASCULAR CONTRAST MEDIA

Procedure	No. of Patients Examined	No. of Patients with Reactions	No. of Patients No Rx*	No. of Patients Rx*	No. of Patients Rx Hospital*	No. of Fatal Reactions
<i>Shehadi Series</i>						
Excretory urography	146,904	7,489	4,994	2,433	52	10
Intravenous cholangiography	6,628	693	409	263	19	2
Cerebral angiography	11,726	231	157	68	5	1
Angiocardiography	7,239	145	55	71	17	2
Aortography	21,506	552	275	256	21	0
Other arteriography	2,460	81	69	11	1	0
Venography	4,881	141	93	46	2	0
Total	201,344	9,332	6,052	3,148	117	15
<i>Toniolo Series</i>						
Excretory urography	67,129	2,768	2,198	514	54	2
Intravenous cholangiography	27,150	1,983	1,549	417	17	0
Cerebral angiography	1,045	32	21	9	2	0
Angiocardiography	672	34	19	9	6	0
Aortography	3,379	113	74	25	13	1
Other arteriography	355	20	15	1	4	0
Venography	1,009	19	15	1	3	0
Total	100,739	4,969	3,891	976	99	3

\* No Rx = mild reaction; no treatment needed, e.g., flushing, nausea, vomiting, "lightheadedness," slight difficulty in breathing, or mild urticaria. These patients were observed until the reaction subsided. (Minor reactions should not be taken lightly. They may herald the advent of severe, life-threatening, or even fatal reactions.)

Rx = moderate reaction; treatment, when needed, was administered in the radiology department and recovery was complete, e.g., urticaria, facial edema, bronchial spasm, laryngeal edema, or a drop in blood pressure (transitory or mild). The patient left the department following the examination.

Hospital Rx = reaction severe enough to require hospitalization, e.g., a prolonged drop in blood pressure, circulatory collapse, chest pain, angina, myocardial infarction, ventricular fibrillation, convulsions, coma, or paralysis. A few patients with severe urticaria or facial or laryngeal edema lasting up to 24 hours or longer were admitted to the hospital or recovery room for observation and treatment and were discharged after all symptoms disappeared.

Fatal reactions were preceded by nausea, vomiting, sneezing, difficulty in breathing, a drop in blood pressure, cyanosis, pulmonary edema, circulatory collapse, ventricular and/or atrial fibrillation, convulsions, acute anuria, and/or respiratory or cardiac arrest.

TABLE IV: SEX DISTRIBUTION

Sex	Series	No. of Patients Examined	No. of Patients with Reactions	Incidence of Reactions
Male	Shehadi	101,305	4,647	4.59%
	Toniolo	52,091	2,616	5.02%
	Total	153,396	7,263	4.73%
Female	Shehadi	100,039	4,685	4.68%
	Toniolo	48,648	2,353	4.83%
	Total	148,687	7,038	4.73%
Total		302,083	14,301	4.73%

TABLE V: AGE DISTRIBUTION OF THE INCIDENCE OF REACTIONS

Age (yr.)	No. of Patients Examined	No. of Patients with Reactions	Incidence of Reactions	Data Missing
<i>Shehadi Series</i>				
0-20	24,229	930	3.84%	
21-35	35,821	2,181	6.09%	
36-50	49,161	2,238	4.55%	
51-65	54,523	2,449	4.50%	
66-100	37,610	1,534	4.07%	
Total	201,344	9,332	4.63%	
<i>Toniolo Series</i>				
0-20	9,447	486	5.20%	
21-30	12,552	625	4.97%	
31-40	13,009	647	4.98%	
41-50	20,364	1,112	5.46%	
51-60	20,180	971	4.82%	
61-70	14,393	708	4.92%	
71-100	10,764	434	4.03%	
Total	100,709	4,983	4.96%	30

TABLE VI: WEIGHT DISTRIBUTION OF THE INCIDENCE OF REACTIONS

Weight (kg)	No. of Patients Examined	No. of Patients with Reactions	Incidence of Reactions
<i>Shehadi Series</i>			
0-30	2,298	72	3.13%
31-45	1,927	81	4.20%
46-60	14,862	738	4.96%
61-75	33,254	1,523	4.57%
76-90	28,791	1,417	4.92%
91-105	11,724	685	5.84%
106-120	3,896	190	4.87%
>120	2,084	106	5.08%
Total	98,836*	4,812	4.86%
<i>Toniolo Series</i>			
0-30	1,957	115	5.89%
31-50	11,984	645	5.41%
51-70	54,231	2,702	4.98%
≥71	32,567	1,506	4.63%
Total	100,739	4,968	4.96%

\* Weight was not indicated in all reports, hence the difference between the total in this table and the 201,344 given in TABLE I.

TABLE VII: INCIDENCE OF REACTIONS IN PATIENTS WITH A HISTORY OF ALLERGY

	No. of Patients with Allergy	No. of Patients with Reactions	Incidence of Reactions
Shehadi	8,465	1,011	11.94%
Toniolo	7,998	896	11.20%
Total	16,463	1,907	11.58%

Shehadi series for urography and approximately 3% fewer for cholangiography, in the arterial studies the incidence of reactions was persistently higher among Toniolo's cases (TABLES II and III).

**Fatal Reactions:** Not counting deaths attributed to primary disease or technique, there were 18 fatal reactions out of 302,083 examinations (0.006%) (TABLES II and III). Of these, 11 occurred during excretory urography, 2 during intravenous cholangiography, 2 during angiocardiology, and 1 each during cerebral angiography, aortography, and venography. A detailed study and critical evaluation of fatal reactions will be the subject of a forthcoming report.

*Influence of Sex, Age, Weight, and Allergy*

The incidence of adverse reactions was the same for both sexes and practically identical in both series (TABLE IV). However, there was a small difference between the two series in the younger age groups; the rate was 3.84% in the Shehadi series (TABLE V)—which is closer to the 3.4% reported by Gooding *et al.* (2)—and 5.20% in the Toniolo series (TABLE V). Most patients were in their third or fourth decade.

Only in the lower weight group was there any significant

difference in the incidence of adverse reactions (TABLE VI); this corresponds to the lower age group already discussed above, in which the rate was slightly higher in the Toniolo series. Italian children tend to eat meals rich in carbohydrates (3), which explains the difference in weight but does not account for the difference in the incidence of reactions. Other contributing factors cannot now be identified.

Correlation with allergy showed no significant difference between the two series, though the rate was slightly lower in the Toniolo series (TABLE VII). The incidence for the combined series was 11.58%, or roughly twice that of the general population. In the Shehadi survey, the incidence has varied between 10.00% and 12.5% during various reporting periods.

## SUMMARY AND CONCLUSIONS

Based on the data collected in our prospective survey, there is no significant racial or geographic difference in the incidence of adverse reactions to intravascular contrast media. The overall incidence was at or slightly below the 5% level; and we could find no differences related to sex, age, or weight save for a slight variance in the lower age and weight groups, with the incidence being slightly higher in the Toniolo series. To broaden the geographic base of our study, we hope to be able to conduct a prospective survey in Asia, Africa, and South America at a future date.

**ACKNOWLEDGMENTS:** We offer our deep appreciation and gratitude to the many colleagues who, notwithstanding the heavy demands made on them in the conduct of their daily work, gave generously of their time and effort in support of the work of the Committee. Outside the United States, the following colleagues have conducted and/or directed the study in their respective countries: Dr. Geoff Benness (Australia), Dr. Jean DeBacker (Belgium), Drs. Douglas MacEwan and Harald Stolberg

(Canada), Dr. Per Amundsen (Norway), Prof. Erik Boijesen (Sweden), and Dr. Ivo Obrez (Yugoslavia).

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