

Selection of contrast media

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A generation of angiographers have witnessed the development of new and improved contrast agents. For a quarter of a century, contrast media available for radiological studies have been salts of iodinated organic acids. The structural formula consists of a benzene ring, iodine atoms, side chains (anions), and sodium, calcium, magnesium, or meglumine salts (cations).

With advances in the basic understanding of the available contrast agents in the 1950s and the demonstration of safe and satisfactory intravascular studies in animals and humans, deliberate efforts to visualize the coronary artery circulation by nonselective and selective techniques were attempted by several investigators.¹⁻⁶ After fear of serious ventricular arrhythmias secondary to transient myocardial ischemia and other serious adverse reactions had been challenged successfully, and selective coronary arteriography became the technique of choice, a search for contrast media followed that would improve opacification and at the same time provide patient safety.

The original experience in the performance of cine coronary arteriography in 1020 patients at the Cleveland Clinic with Hypaque 90 and Cardiografin 85 was reported in 1962.⁷ Only major complications were recorded. Ventricular fibrillation

Table 1. Contrast media; characteristics and complications (July 1, 1960 to June 30, 1962)

Product	Anion	Cation(s)	Conc, %	Na, mEq/ml*	I ₂ , mg/ml	No. of studies†	Complication rate, %
Cardiografin 85	Diatrizoate	Meglumine	85	...	400	596 (319)	1.7
Cardiografin 64-70	Diatrizoate	Meglumine	64-70	...	300-329	56 (46)	5.4
Conray 60	Iothalamate	Meglumine	60	...	282	31 (16)	13.0
Angio Conray	Iothalamate	Sodium	80	1.25	480	5 (3)	0
Hypaque 90	Diatrizoate	Meglumine (60%) Sodium (30%)	90	0.47	462	585 (370)	0.3
Hypaque 65-70	Diatrizoate	Meglumine (44%-47%) Sodium (21%-23%)	65-70	0.33-0.36	333-359	81 (72)	5.0
Renovist	Diatrizoate	Meglumine (34.3%) Sodium (35%)	70	0.58	372	(26)	11.5

* Serum sodium, 0.14 mEq/ml.

† Number of coronary arteriographic studies in parentheses.

occurred in 12 patients (1.2%), and two deaths (0.19%) were probably related to the injection of contrast media. For comparison, angiographic studies with and without selective coronary arteriograms performed with these and other agents between July 1, 1960 and June 30, 1962 were reviewed. Results of some of the studies are included in the original report. The characteristics of the agents and the incidence of major adverse reactions attributed to each are shown in *Tables 1 and 2*. Studies performed with Cardiografin (concentration of methylglucamine salts greater than 70%) were associated with fewer complications. During the same period, other investigators demonstrated that agents with a high percentage of methylglucamine were associated with a low incidence of major complications.⁸⁻¹¹ No conclusion can be derived from the small experience (five patients) with sodium salts of iothalamate (Angio Conray), but Gensini and DeGiorgi¹² found the agent to be hazardous.

The administration of contrast agents consisting of combinations of methylglucamine and sodium salts produced varying responses. Like Cardiografin, the concentration of methylglucamine seems to play an important role. The lack of methylglucamine salts (< 50%) was associated with a higher incidence of complications (*Table 1*).

Meglumine diatrizoate 66% and sodium diatrizoate 10% (Renografin 76)* had been used for angiocardiology and selective coronary arteriography for many years. In 1976, Gensini and Kelly¹³ reported less than 0.07% incidence of significant morbidity (uncontrolled hypotension, myocardial infarction or death) in 723 coronary arteriographic studies. This report and a recent experience in 1236 patients would support the use of this contrast medium for evaluation of the central circulation (*Table 3*).

* Other characteristics: Na (mEq/ml) 0.19, I₂ (mg/ml) 370.

Table 2. Contrast media; complications (July 1, 1960 to June 30, 1962)

Product	Total no. of studies	Complications	No. of studies	Percent
Cardiografin 85	596 (319)	Supraventricular tachycardia	1	0.2
		Sinus bradycardia	1	0.2
		Asystole	1	0.2
		Ventricular fibrillation	5	0.8
		Death	2	0.3
Cardiografin 64-70	56 (46)	Nausea and vomiting*	1	1.7
		Transient heart block	1	1.7
		Ventricular fibrillation	1	1.7
Conray 60	31 (16)	Neurologic (transient)*	2	6.4
		Transient heart block	1	3.2
		Ventricular fibrillation	1	3.2
Angio Conray	5 (3)
Hypaque 90	585 (370)	Asystole	1	0.2
		Ventricular fibrillation	1	0.2
Hypaque 65-70	81 (72)	Atrial fibrillation	1	1.2
		Asystole	1	1.2
		Ventricular fibrillation	2	2.4
Renovist	(26)	Ventricular fibrillation	3	11.5

Number of coronary arteriographic studies in parentheses.

* Cerebral angiographic study.

Recently, meglumine iothalamate 52% and sodium iothalamate 26% (Vas-coray)† were evaluated in 1022 patients. The incidence of complications is listed in *Table 4*.

Other contrast media have been used, but little differences have been reported. Grainger¹⁴ found agents with metrizoic acids (Triosil and Isopaque) to be similar to the diatrizoate and iothalamate salts. Others concerned with the hemodynamic actions of sodium meglumine diatrizoate believe a non-ionic contrast material, metrizamide or ionic agent (sodium meglumine calcium metrizoate-Isopaque 440) to be the best for coronary arteriography.¹⁵ Zipfel et al¹⁶ have suggested that the addition of Ca⁺⁺ to ionic contrast media may be beneficial in high risk patients. Particulate contrast media suggested by Mygind¹⁷ for assessing cardiovascular he-

Table 3. Renografin 76; complications (1236 patients)

Reactions	No. of patients	Percent
Gastrointestinal (nausea and vomiting)	80	6.4
Chills	7	0.6
Allergic		
urticaria	105	8.5
angioneurotic edema	3	0.2
Hypotension*	34	2.8
Neurologic (transient)	4	0.3
Arrhythmia	61	5.0
Sinus bradycardia†	40	3.2
Transient asystole‡	5	0.4
Asystole‡	2	0.2
Supraventricular arrhythmia	5	0.4
Ventricular tachycardia	6	0.5
Ventricular fibrillation	3	0.2
Death	0	

* Required Levophed.

† Required atropine.

‡ Required massage.

modynamics has not been widely accepted.

In the selection of a contrast agent for visualization of cardiac structures, the choice must be based on the balance between toxicity and radiographic effi-

† Other characteristics: Na (mEq/ml) 0.41, I₂ (mg/ml) 400.

Table 4. Vascoray; complications (1022 patients)

Reactions	No. of patients	Percent
Gastrointestinal (nausea and vomiting)	46	4.5
Chills	3	0.3
Allergic		
urticaria	71	7.0
angioneurotic edema	4	0.4
Hypotension*	13	1.3
Neurologic (transient)	4	0.4
Arrhythmia	115	11.2
Sinus bradycardia†	61	6.0
Transient asystole‡	26	2.5
Asystole‡	4	0.4
Supraventricular arrhythmia	11	1.1
Ventricular tachycardia	5	0.5
Ventricular fibrillation	8	0.8
Death	0	0

* Required Levophed.

† Required atropine.

‡ Required massage.

ciency. In the past 25 years, progress has been slow, but the introduction of triiodinated compounds derived from the benzoic acid ring has been an improvement. Viscosity and iodine content are important, but the selection seems to depend mainly on the anionic or cationic characteristics. The most acceptable agents in terms of myocardial toxicity seem to be the meglumine sodium diatrizoate or iothalamate combination when the concentration of methylglucamine or methylglucamine and sodium concentration is greater than 70% and the ratio of methylglucamine to sodium is 2:1 or greater (Hypaque 90, Renografin 76, and Vascoray). Methylglucamine diatrizoate 85% (Cardiografin) was associated with a slight increase in cardiac toxicity and like Hypaque 90 is difficult to use because of the high viscosity. Each of these agents provides satisfactory radiopacity.

The best of the agents discussed are acceptable by current standards, but a search for new and improved contrast media should continue.

References

1. DiGuglielmo L, Guttadauro M: Anatomic variations in the coronary arteries; an arteriographic study in living subjects. *Acta Radiol* **41**: 393-416, 1954.
2. Thal AP, Lester RG, Richards LS, et al: Coronary arteriography in arteriosclerotic disease of the heart. *Surg Gynecol Obstet* **105**: 457-464, 1957.
3. Dotter CT, Frische LH: Visualization of the coronary circulation by occlusion aortography: a practical method. *Radiology* **71**: 502-523, 1958.
4. Lehman JS, Boyer RA, Winter FS: Coronary arteriography. *Am J Roentgenol* **81**: 749-763, 1959.
5. Sones FM Jr, Shirey EK, Proudfit WL, et al: Cine-coronary arteriography (abstr). *Circulation* **20**: 773-774, 1959.
6. Judkins MP: Selective coronary arteriography; Part I. A percutaneous transfemoral technic. *Radiology* **89**: 815-824, 1967.
7. Sones FM Jr, Shirey EK: Cine coronary arteriography. *Mod Concepts Cardiovasc Dis* **31**: 735-738, 1962.
8. Fischer HW, Eckstein JW: Comparison of cerebral angiographic contrast media by their circulatory effects: an experimental study. *Am J Roentgenol* **86**: 166-177, 1961.
9. Lehman JS: High concentrations of diatrizoate methylglucamine. *Ann New York Acad Sci* **78**: 943-955, 1959.
10. Guzman, SV, West JW: Cardiac effects of intracoronary arterial injections of various roentgenographic contrast media. *Am Heart J* **58**: 597-607, 1959.
11. Tapia FA, Bolton HE, Mazel MS: Selective coronary cine-arteriography. An improved method for visualization of the coronary arteries. *Angiology* **12**: 46-51, 1961.
12. Gensini GG, De Giorgi S: Myocardial toxicity of contrast agents used in angiography. *Radiology* **82**: 24-33, 1964.
13. Gensini GG, Kelly AE: Reassessment of contrast agent for coronary angiography. *Curr Ther Res* **19**: 631-636, 1976.
14. Grainger RG: Future prospects in diagnostic radiology. *Proc R Soc Med* **64**: 243-251, 1971.
15. Higgins CB, Schmidt W: Direct and reflex myocardial effects of intracoronary administered contrast materials in the anesthetized and conscious dog: comparison of standard and newer contrast materials. *Invest Radiol* **13**: 205-216, 1978.

16. Zipfel J, Baller D, Karsch R, et al: Cardiotoxicity of contrast media used in coronary angiography. Decrease by correcting intravascular $\text{Na}^+/\text{Ca}^{++}$ -imbalance. (Abstr) *Circulation* **60**: Suppl II: II-162, 1979.
17. Mygind T: Contrast-loaded gelatin spherules: preliminary report on a new particulate radiographic contrast medium for experimental flow pattern studies. *Radiology* **86**: 138-140, 1966.