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Choice of contrast medium in sialography

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Contrast media used for sialography were originally developed for other medical applications. Therefore, it was considered desirable to investigate the properties of these substances for use in sialography. Eleven radiopaque substances were selected, and their properties for sialography were studied. An in vitro study was made to determine their contrast qualities and their rate of evacuation after the sialographic examination. In animal experiments the possible harmful effects of the media on salivary gland tissues were studied. Moreover, the effects of the radiopaque material on the extraglandular tissues—which are important in understanding the consequences of spilling into these tissues—were investigated. The results of this study were compared with data from the literature. Conray 80, Amipaque 440, Lipiodol UF, Myodil, and Duroliopaque appear to be the media most suited for sialography, provided glandular overfilling is avoided. A prolonged clinical study is advised for a further selection from these agents.

Contrast media used in sialography were originally developed for radiologic examination other than the study of salivary glands. The radiopaque materials in general use for sialography can be divided into oily media, water-soluble media, and suspensions. The literature regarding the properties and the side effects of these media in the indicated fields of application is very extensive (Tables I and II). However, the conclusions concerning side effects are sometimes contradictory.

The use of some of the media in sialography has resulted in many publications (Table II) in which the conclusions on side effects are also controversial. The literature is also incomplete, especially concerning some recently developed radiopaque materials. This diversity of opinions was the reason for the present investigation in which the properties of a number of contrast media, of potential use in sialography, are

compared. The criteria for the evaluation of the contrast media were as follows:

1. The iodine salt concentrations before and after dilution with saliva should be sufficiently high.
2. The media should be eliminated rapidly from the healthy salivary gland after sialography. This property permits study of the glandular function and diminishes the risk of local side effects. It also makes possible the investigation of more than one gland during the same session.
3. The contrast media should have no harmful effects on the salivary gland tissue.
4. The media should be harmless in the event of spilling into the extraglandular tissues (fausse route).

MATERIALS AND METHODS

Information on the contrast media selected for this investigation is given in Tables I and II.

The iodine salt concentrations as given by the manufacturer or from the literature were checked radiographically. The iodine salt content was determined densitometrically from radiographs made from undiluted contrast medium samples by compar-

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Fig. 1. Sialogram of a rabbit's submandibular gland; normal filling with 0.2 ml of a water-soluble contrast medium.

Fig. 2. Sialogram of a rabbit's submandibular gland; overfilling with 0.4 ml of an oily contrast medium.

Table I

Product name	Generic name	Water soluble/oily	mg I/ml		Viscosity (stated) at 37° C in mPa.s	Osmolality (stated) at 37° C in mmol/kg water
			Stated	Measured		
Conray 80	Na-iodalamate	W	480	478	8 (37.5° C)	3,140
Isopaque 440	Na(+Ca+Mg)-metrizoate	W	440	442	6.6	2,640
Amipaque	Metrizamide	W	440*	406	25.6	670
Urombrine 420	Meglumine+Na-diatrizoate	W	420	406	6—7	1,885†
Urografin 76%	Meglumine+Na-diatrizoate	W	370	346	8.9	2,100
Endografin	Meglumine-iodipamide	W	350	340	18.7	840
Hytrast	Ioppydol+iopydone	W suspension	500	470	600	—
Dionosil oily	Propylidone	O suspension	340	382	1,250 (?° C)	—
Lipiodol UF	Ethyl diiodostearate	O	480	478	25	—
Myodil	Iophendylate	O	384	370	?	—
Duroliopaque	Ethyl monoiodostearate	O	480	478	12	—

*Powder and liquid volumes mixed according to the manufacturer's instructions for a solution containing 440 mg I/ml.

†Osmolality in mmol/L solution.

ing with potassium iodide solutions of known concentrations. A Joyce, Loebl & Company double-beam recording microdensitometer was used for these and all other density measurements on the radiographs in this study.

Radiographs of a phantom model were made for the determination of the tendency of the contrast media to be diluted by saliva in a glandular duct.⁴⁶ The phantom used to simulate a human head was composed of fourteen layers (25 × 25 cm) of Plexiglas, each 1 cm thick, and four sheets of aluminum,

each 0.1 cm thick. Along the film side of the phantom model, perpendicular to the x-ray beam, a polyethylene tube was placed in a horizontal position. The tube had an inner diameter of 2 mm and was comparable to a glandular duct of mean width.

Adjacent to the tube, an aluminum step-wedge (3-6-9-12-17 mm) was placed as reference object for densitometric measurements. The secretory pressure of a stimulated salivary gland was simulated by connecting one end of the tube to an open-ended 20

Fig. 3. Radiographs used for the study of contrast medium dilution with artificial saliva in a polyethylene tube. The radiographs were made immediately after the contrast medium instillation (t_1) and 1 (t_2) and 5 (t_3) minutes later. Contrast medium: Urombrine 420.

Fig. 4. See legend for Fig. 3. Contrast medium: Hytrast.

cc syringe placed 65 cm above the horizontal part of the tube in the phantom.⁴⁷ This reservoir and tube system was filled with artificial saliva at a temperature of 37°C. The composition of this artificial saliva is given in the appendix. The other end of the horizontal part of the tube was connected to a syringe filled with one of the selected contrast media at 37°C. An amount of contrast medium sufficient to fill one half of the horizontal part of the tube was instilled in 30 seconds. Radiographs were obtained immediately after the instillation (t_1) and 1 minute (t_2) and 5 minutes (t_3) later. The radiographs were processed under standardized conditions. Densitometric measurements were performed on nine predetermined positions along the tube's image. The density at each position was expressed in millimeters of aluminum equivalent of the step wedge. These values were compared with those from radiographs made of the same phantom after filling of the tube with undiluted iodine salt solutions of known concentration. This permitted the determination of the iodine salt concentration for all measuring points of the tube.

To study the evacuation of contrast media from a healthy salivary gland, the same Plexiglas aluminum phantom was used and a portion of the horizontal part of the tube lumen was narrowed to a diameter of 0.2 mm in order to simulate the finer glandular ducts

(Figs. 8 and 9). All other circumstances were the same as described above for the hydrostatic system. A volume of contrast medium sufficient to fill one half the length of the narrowed lumen was instilled (37°C) and then the injecting syringe was removed and the tube end was left open. Radiographs were obtained immediately after removal of the syringe (t_1) and 5 minutes later (t_2). The films were processed under standardized conditions. The density of the tube image was measured at the place of instillation on all films, and the iodine salt concentration was determined as described above.

Animal experiments were conducted to study the local toxicity of the contrast media. All experiments described here were also performed with a physiologic saline solution for control purposes. Rabbits were selected for the study of the influence of radiopaque media on salivary gland tissue. Under general intravenous anesthesia (Nembutal), both submandibular glands of each rabbit were instilled with the same contrast material. One gland was filled with 0.2 ml of the radiopaque material (normal volume), and the other side was overfilled by the instillation of 0.4 ml. For Hytrast and Dionosil oily, both highly viscous suspensions, a maximum of 0.3 ml could be instilled. Oblique lateral radiographs of the glands were made with occlusal dental film immediately after instillation and 5, 30 and (if necessary) 60 minutes later. The radiographs were used to evaluate the amount of glandular filling (Figs. 1 and 2) and evacuation of the contrast material. Seven days after the instilla-

Table II

Contrast medium	Indications (manufacturer)	Application in sialography by:	Side-effects in sialography	Side effects in other applications
Conray 80	Angiography; cavography; sialography; dacryocystography; fistulography	(1) c m of choice; (2)	No	(3) Sodium-containing c m (Conray 80) generally have smaller local tolerance than meglumine combinations
Isopaque 440	Urography; angiography; sialography	(4); (5); (6); (7); (8)	(6) Pain caused by parenchymatous filling; postsialographic glandular swelling during 9 hours caused by the hypertonic c m; (7) rapid hydrolysis and disappearance of c m.	(9; 10) Small reversible side effects in c m study of kidney
Amipaque	Various concentrations for myelography; ventriculography; angiography; cavography	(6)	(6) No pain or parenchymatous filling; postsialographic glandular swelling for 2 hours	Not very irritating in myelography (11) and arthrography (12)
Urombrine 420	Urography; sialography	No	No	No
Urografin 76%	Urography; angiography; hysterosalpingography; sialography	(7); (13) c m of choice (1); (14)	(13) Normal postsialographic glandular function; (15) some postsialographic glandular inflammation during some days; (16) no postsialographic granulomatous reaction	(3; 9; 17) Not very irritating; (15) light inflammation after s c application after 1 day but not after 7 days
Endografin	Hysterosalpingography; urethrography; fistulography; sinusography; atresias; galactography	(18) c m of choice (1); (8); (19)	(16) No postsialographic granulomatous reaction; (19) reversible damage; less subjective complaints than with Urografin, Conray 80 and Isopaque	(17; 20; 21) Locally (very) irritating; (22) toxic after intravenous instillation; (19) reversible damage after s c application during 7 days
Hytrast	Bronchography; laryngography; cystography; fistulography	(23); (24); (25)	(23) Postsialographic c m retention for 3-4 days; (24) no histologic changes of glands after c m retention; (25) long-standing glandular swelling after c m retention	(11; 26 to 31) Postbronchographic c m retention with inflammation and fibrosis; (26) c m retention longer than 10 days and extensive inflammation and fibrosis after s c application

C m = Contrast medium.

S c = Subcutaneous.

tion, the glands were removed with the aid of general anesthesia and radiographed to determine contrast medium retention and processed for histologic evaluation with hematoxylin and eosin staining.

The effects of instillation of contrast media into the subcutaneous soft tissues, a situation comparable to unintentional extravasation in sialography, were studied in rats. Following disinfection of the skin surface, 0.2 ml of each contrast material was injected into the subcutaneous tissue of each rat. Tissues were removed 2, 8, and 70 days later and studied clinically, radiographically for contrast medium retention,

and histologically (hematoxylin and eosin staining). Each material was tested three times.

RESULTS

In vitro experiments

Iodine salt concentration. The determination of the iodine salt content for each of the contrast media investigated are given in Table I. Differences from the stated values exceeding 5% were found for Amipaque (-7.7%), Urografin 76% (-6.5%), Hytrast (-6%), and Dionosil oily (+12.4%).

Dilution effects. Dilution effects were determined

TABLE (cont'd)

Contrast medium	Indications (manufacturer)	Application in sialography by:	Side effects in sialography	Side effects in other applications
Dionosil oily	Bronchography	(32); (33)	(15) c m retention with inflammation and parenchymal degeneration 7 days after sialography; (16) postsialographic granulomatous reaction; (34) the arachis oil in the c m causes inflammation, fibrosis granulomas, and necrosis of stroma, and vacuolation of parenchyma and stroma 3.5 weeks after sialography	(11; 17; 26; 29; 35) Postbronchographic c m retention and chronic inflammation; (15; 26; 36) long-standing retention and moderate-grave inflammation after s c application
Lipiodol UF	Cholangiography; hysterosalpingography; lymphography; sialography	(11); (14) C m of choice (1); (5); (7); (13); (33); (37)	(7; 16; 38; 39) No postsialographic damage after periods between 1 and 300 days; (15) light postsialographic inflammation during some days; (37) chronic inflammation after c m extravasation from parenchyma	(15) C m retention and inflammation for over 14 days after s c application; c m retention results in chronic irritation in bronchography (40; 41); myelography (42; 43), and lymphography (11; 41)
Myodil	Myelography; ventriculography	(5; 32; 44) C m of choice; (1); (7); (8); (33); (45)	(8) Postsialographic granulomata possible; (14; 45) granulomata after c m extravasation from parenchyma; (16) no postsialographic granuloma	(11; 17; 42; 43) Chronic inflammation possible after c m retention; (42) long-standing retention after s c application
Duroliopaque	Myelography; ventriculography	No	No	(42) Chronic irritation after myelography; long-standing retention without irritation after s c application

densitometrically and a decrease of less than 10% from the original iodine salt concentration was classified as small; 10 to 20% as moderate; 20 to 30% as high; and over 30% as very high. Typical radiographs of the horizontal portion of the tube at t_1 , t_2 , and t_3 for Urombrine 420 and Hytrast are shown in Figs. 3 and 4. Graphs of the iodine salt concentration at different sites for the time intervals and contrast media mentioned are shown in Figs. 5 and 6. In these figures a progressive dilution of Urombrine 420 along the length of the tube and with time can be seen. The iodine salt concentration after initial and prolonged dilution of the media is presented graphically in Fig. 7. The oily media showed no dilution, and this resulted in moderate to very high iodine salt concentrations at t_1 , t_2 , and t_3 .

The initial dilution (t_1) of the other media was *moderate to high* for Isopaque 440, Urombrine 420,

and Urografin 76%; *high* for Conray 80 and Hytrast; *high to very high* for Amipaque and Endografin. The highest iodine salt concentrations with these media were found for Conray 80, Isopaque 440, Hytrast, and Urombrine 420. Both Amipaque and Endografin demonstrated low to very low iodine salt concentrations in spite of their relatively high viscosity and low osmolality.

Prolonged dilution of water-soluble media halfway along the tube at t_2 (1 minute) was determined densitometrically, and a decrease smaller than 10% relative to the iodine salt concentration at t_1 was classified as small; 10 to 20% as moderate; 20 to 30% as high; and over 30% as very high. Prolonged dilution at t_2 was *small* for Isopaque 440, Amipaque, and Hytrast; *moderate* for Urombrine 420 and Endografin; *high* for Conray 80; and *very high* for Urografin 76%.

Fig. 5. Graphic presentation of the iodine salt concentration (mgI/ml) at different sites of the polyethylene tubes from Fig. 3 for the time intervals mentioned. Contrast medium: Urombrine 420.

Fig. 6. Graphic presentation of the iodine salt concentration (mgI/ml) at different sites of the polyethylene tubes from Fig. 4 for the time intervals mentioned. Contrast medium: Hytrast.

Prolonged dilution halfway along the tube at t_3 (5 minutes) was *small* for Hytrast; *moderate* for Amipaque; *high* for Conray 80, Isopaque 440, and Endografin; and *very high* for Urombrine 420 and Urografin 76%.

The absolute iodine salt concentration of the water soluble media at t_2 and t_3 was most favorable for Hytrast (moderate) and for Conray 80 and Isopaque 440 (low). Dilution of the other water-soluble media resulted in very low iodine salt concentrations. The most favorable results in the dilution experiments

were successively found for Lipiodol UF, Dionosil oily, Myodil, Duroliopaque, Hytrast, Conray 80, and Isopaque 440.

Evacuation of contrast media. Typical radiographs of the narrow lumen in tubes filled with Isopaque 440 and Lipiodol UF in the evacuation study are shown in Figs. 8 and 9. The results of the evacuation study for all media are given in Table III. Most of the water-soluble media show an almost complete evacuation in 5 minutes. Amipaque and Hytrast were evacuated much slower, probably as a

Fig. 7. Iodine salt concentration (mgI/ml) after initial (t_1) and prolonged (t_2 and t_3) dilution of the contrast media. 1 = Undiluted contrast medium; 2 = at instillation place at t_1 (=0 min); 3 = halfway along the tube at t_1 (=0 min); 4 = halfway along the tube at t_2 (=1 min); 5 = halfway along the tube at t_3 (=5 min). An iodine salt concentration smaller than 250 mg/ml was classified as very low; 250 to 300 mg/ml, low; 300 to 350 mg/ml, moderate; 350 to 400 mg/ml, high; over 400 mg/ml, very high.

Fig. 8. Radiographs used for the study of contrast medium evacuation from a polyethylene tube with a localized narrowing at t_1 (=0 min) and t_2 (=5 min). Contrast medium: Isopaque 440. At t_2 the evacuation is almost complete.

Fig. 9. See legend for Fig. 8. Contrast medium: Lipiodol UF. At t_2 the contrast medium has moved slightly toward the instillation point (*left*) as a result of the hydrostatic pressure (*right*): incomplete evacuation.

Fig. 10. Photomicrograph of rabbit submandibular gland removed 7 days after sialography with 0.4 ml Endografin (overfilling). Some fibrosis of the parenchyma, hyperemia, and extensive invasion with lymphocytes and macrophages are visible. (Hematoxylin and eosin stain. Magnification, $\times 40$.)

result of their higher viscosity. The same is true for the oily media except for Duroliopaque, which was almost completely evacuated in 5 minutes.

The low-viscosity water-soluble media and Duroliopaque seem more suited for the study of salivary gland function than the more viscous media.

In vivo experiments

Evacuation of contrast media. Results of the evacuation of contrast media after sialography in rabbits are given in Table IV. Radiographs made 30 minutes after sialography showed complete evacuation in both normally filled and overfilled glands for

most of the water-soluble media. The suspensions and the oily media had longer retention times, and in the case of overfilled glands retention was found for most of these media after 7 days.

Tissue reaction after normal glandular filling. Results of the histologic evaluation of the submandibular glands removed 7 days after sialography are presented in Table V. Histologic changes occurred following normal glandular filling with six of the tested contrast media. No abnormalities were seen after sialography with Amipaque, Urografin 76%, Lipiodol UF, Myodil, and Duroliopaque. Some ductectasia was visible with Conray 80. Postsialographic

Fig. 11. Photomicrograph of rabbit submandibular gland removed 7 days after sialography with 0.4 ml Lipiodol UF (overfilling). Note destruction of the parenchyma, resulting in contrast-medium vacuoles surrounded by macrophages. (Hematoxylin and eosin stain. Magnification, $\times 15$.)

Table III Evacuation of the contrast media after 5 minutes (t_g)*

Contrast medium	Over 95%	5-10%	Less than 5%
Conray 80	x		
Isopaque 440	x		
Amipaque		x	
Urombrine 420	x		
Urografin 76%	x		
Endografin	x		
Hytrast			x
Dionosil oily			x
Lipiodol UF			x
Myodil		x	
Duroliopaque	x		

*Decrease in the iodine salt concentration at t_2 relative to t_1 in percent.

glandular fibrosis and/or the presence of inflammatory cells occurred with the other media; in order of increasingly severe tissue reactions, these media are Dionosil oily, Urombrine 420, Isopaque 440, Endografin, and Hytrast. In addition to these changes, some glandular necrosis was found after the instillation of Hytrast. Some of the observed stromal abnormalities probably resulted from the extravasation of contrast media into the stroma.⁴⁸

Tissue reaction after glandular overfilling. Glandular overfilling resulted in histologic changes with all media. Some glandular fibrosis and/or the presence of inflammatory cells occurred with Amipaque,

Table IV

Contrast medium	Volume (ml)	5 min	30 min	60 min	1 week
Conray 80	0.2	+	-	-	-
	0.4	+	-	-	-
Isopaque 440	0.2	+	-	-	-
	0.4	+	-	-	-
Amipaque	0.2	+	-	-	-
	0.4	+	±	-	-
Urombrine 420	0.2	+	-	-	-
	0.4	+	-	-	-
Urografin 76%	0.2	+	-	-	-
	0.4	+	-	-	-
Endografin	0.2	+	-	-	-
	0.4	+	±	-	-
Hytrast	0.2	+	+	+	-
	0.3*	+	+	+	+
Dionosil oily	0.2	+	+	±	-
	0.3*	+	+	+	-
Lipiodol UF	0.2	+	+	-	-
	0.4	+	+	+	+
Myodil	0.2	+	+	-	-
	0.4	+	+	+	+
Duroliopaque	0.2	+	+	-	-
	0.4	+	+	+	+

- = Complete elimination; ± = slight retention; + = retention.

*A maximum of 0.3 ml of this (viscous) medium could be injected.

Isopaque 440, Urografin 76%, and Conray 80. These changes were more pronounced, and sometimes accompanied by localized necrosis, with Endografin (Fig. 10), Urombrine 420, Dionosil oily, and Hytrast. Extensive destruction of the parenchyma

Fig. 12. Photomicrograph of rabbit submandibular gland removed 7 days after sialography with 0.4 ml Duroliopaque (overfilling). Extensive vacuolation and destruction of the parenchyma and infiltration with neutrophils are visible. (Hematoxylin and eosin stain. Magnification, $\times 150$.)

Table V

Contrast medium	Normal filling (0.2 ml)	Overfilling (0.4 ml)
Physiologic saline	Normal	Normal
Conray 80	Some ductectasia	Some fibrosis of parenchyma and invasion with lymphocytes, plasma cells, and macrophages; also fibrosis of stroma
Isopaque 440	Some fibrosis of parenchyma and invasion with a few lymphocytes	Same as with 0.2 ml
Amipaque	Normal	Stromal invasion with a few neutrophils
Urombrine 420	Some fibrosis of stroma	Moderate to grave fibrosis of parenchyma and invasion with some lymphocytes and neutrophils
Urografin 76%	Normal	Localized fibrosis at glandular periphery and some invasion with neutrophils
Endografin	Some fibrosis of parenchyma, hyperemia, and invasion with lymphocytes and neutrophils	Some fibrosis of parenchyma, more hyperemia, and extensive invasion with lymphocytes and macrophages (Fig. 10)
Hytrast*	Fibrosis of parenchyma and invasion with lymphocytes and neutrophils; some stromal necrosis, extending into parenchyma and moderate invasion with macrophages	Same as with 0.2 ml
Dionosil oily*	Hyperemia and some invasion of stroma with macrophages and neutrophils	Same as with 0.2 ml and, in addition, localized necrosis within the stroma
Lipiodol UF	Normal	Parenchymal destruction resulting in c m vacuoles surrounded by macrophages (Fig. 11)
Myodil	Normal	Extensive parenchymal vacuolation and invasion with lymphocytes and some neutrophils
Duroliopaque	Normal	Extensive parenchymal vacuolation and extensive invasion with neutrophils (Fig. 12)

*A maximum of 0.3 ml of this viscous medium could be instilled into the salivary gland.

and the formation of contrast medium vacuoles were found after glandular overfilling with Lipiodol UF (Fig. 11), Myodil, and Duroliopaque (Fig. 12).

Subcutaneous reactions. Results for the subcuta-

neous injection of contrast medium in rats are given in Table VI. Radiographically visible contrast medium retention was found in varying degrees with the suspensions and all oily media in the 2- and 8-day

Table VI

Contrast medium	Clinical induration (days)			Radiographic c m retention (days)			Histological inflammation and/or c m retention (days)		
	2	8	70	2	8	70	2	8	70
Physiologic saline	-	-	-	-	-	-	-	-	-
Conray 80	±	-	-	-	-	-	++; Lymphocytes, macrophages and neutrophils; some necrosis of musculature	++; Some fibrosis; some lymphocytes and macrophages	-
Isopaque 440	±	±	-	-	-	-	++; Some lymphocytes	+/+++; C m vacuoles and lymphocytes	-
Amipaque	-	-	-	-	-	-	-	-	-
Urombrine 420	-	-	-	-	-	-	++; Some lymphocytes	+++; C m vacuoles; moderate infiltrate of macrophages	-
Urografin 76%	-	±	-	-	-	-	-	+++; C m vacuoles; moderate infiltrate of macrophages (Fig. 13)	-
Endografin	±	±	-	-	-	-	++/+; Moderate infiltrate of neutrophils	++; Some lymphocytes some necrosis of musculature	-
Hytrast	++++	++	+++++	+++++	++	++	++++; Retained c m; granulation tissue; many macrophages and neutrophils	+++; Slightly decreased reaction; lymphocytes, neutrophils, macrophages, fibrosis	++; Retained c m with connective tissue capsule; some lymphocytes and macrophages (Fig. 15)
Dionosil oily	±	-	-	+	+	-	++; Retained c m; neutrophils	+++; C m vacuoles with moderate infiltrate of lymphocytes and macrophages (Fig. 14)	-
Lipiodol UF	-	±	-	++	++	-	-	++; C m vacuoles with some lymphocytes and macrophages	-
Myodil	-	±	-	++	++	-	+ C m vacuoles with lymphocytes and macrophages	+++; Same reaction, somewhat more pronounced	-
Duroliopaque	-	-	-	+	+	+	++; Some lymphocytes and macrophages	++; c m vacuoles	++; C m vacuoles surrounded by macrophages

- = No abnormalities present.

± / + / ++ / +++ / ++++ = Abnormalities found in various degrees.

skin tissue specimens. Radiographs of the 70-day specimens only showed retained Hytrast and Duroliopaque.

Clinical and/or histologic abnormalities were found in specimens at 2 and 8 days for all media except Amipaque. All specimens that showed clinical induration also demonstrated histologically visible changes. In order of increasing harmfulness after subcutaneous injection, these media are Conray 80, Lipiodol UF, Endografin, Isopaque 440, Duroliopaque,

paque, Urografin 76% (Fig. 13), Urombrine 420, Myodil, Dionosil oily (Fig. 14), and Hytrast. The 70-day skin tissue specimens only showed abnormalities for Hytrast (Fig. 15) and Duroliopaque.

DISCUSSION AND CONCLUSIONS

The properties of the tested contrast media are summarized in Table VII. Of the water-soluble media evaluated, Conray 80 seems to be the most suited for use in sialography. Amipaque, with its low

Fig. 13. Photomicrograph of rat skin tissue removed 8 days after subcutaneous injection of 0.2 ml Urografin 76%. Contrast-medium vacuoles and a moderately dense infiltrate of macrophages are visible in the subcutaneous tissue. (Hematoxylin and eosin stain. Magnification, $\times 15$.)

Table VII

Contrast medium	Iodine salt concentration after initial (a) and prolonged (b) dilution		C m evacuation in vitro (a) and in vivo after normal filling (b) overfilling (c)			Effect on salivary gland tissue after normal filling (a) and overfilling (b)		Effect on subcutaneous tissues
	a	b	a	b	c	a	b	
Conray 80	+	-	++	+	+	$\pm$	-	-
Isopaque 440	$\pm$	-	++	+	+	-	-	- to --
Amipaque	-	--	-	+	$\pm$	+	-	+
Urombrine 420	$\pm$	--	++	+	+	-	--	- to --
Urografin 76%	-	--	++	+	+	+	-	- to --
Endografin	--	--	++	+	$\pm$	-	--	-- to -
Hytrast	$\pm$	$\pm$	--	-	--	--	--	--
Dionosil oily	+	+	--	-	-	-	--	--
Lipiodol UF	++	++	--	$\pm$	--	+	---	-
Myodil	+	+	-	$\pm$	--	+	---	- to --
Duroliopaque	$\pm$	$\pm$	++	$\pm$	--	+	---	--

Plus values = Favorable properties.

Minus values = Unfavorable properties.

osmolality and relatively high viscosity, is much less radiopaque after dilution. Isopaque 440 is more noxious than the two water-soluble media previously mentioned. Of the oily media investigated, Lipiodol UF is best suited for sialography; Myodil and Duroliopaque are less radiopaque. The relatively low viscosity of Duroliopaque seems to be a favorable property of this medium. In the assessment of these results, however, it should be remembered that, in vivo, the elimination of water-soluble media occurs as a result of excretion from and resorption by the

salivary gland. In this experiment only the role of excretion in the elimination of contrast media could be tested. Further studies should be performed in vivo.

It should be stressed that in sialography glandular overfilling should be avoided even with the most suitable contrast media mentioned above. Other recommendations for optimum results in sialography are as follows:

The use of a water-soluble medium requires that radiographs be made as soon as possible after instil-

Fig. 14. Photomicrograph of rat skin tissue removed 8 days after subcutaneous application of 0.2 ml Dionosil oily. Contrast-medium vacuoles with a moderately dense infiltrate of lymphocytes and macrophages extending between the musculature are visible in the subcutaneous tissue. (Hematoxylin and eosin stain. Magnification, $\times 15$.)

Fig. 15. Photomicrograph of rat skin tissue removed 70 days after subcutaneous application of 0.2 ml Hytrast. Retained contrast medium, surrounded by a connective tissue capsule and some lymphocytes and macrophages, is visible in the subcutaneous tissue. (Hematoxylin and eosin stain. Magnification, $\times 40$.)

lation of the medium. This is necessary to limit dilution and resorption of the medium, thus avoiding a decrease in the radiopacity of the sialogram.

Low-viscosity media make possible the study of glandular function (contrast medium evacuation studies).

The use of image intensifier fluoroscopy⁴⁹ can be of value in the prevention of glandular overfilling during sialography.

Image intensifier fluoroscopy during sialography also helps to prevent the spilling of large amounts of contrast medium into the extraglandular tissues (fausse route).

The foregoing results and conclusions were based on in vitro studies and animal experiments; a prolonged clinical investigation of Conray 80, Amipaque 440, Lipiodol UF, Myodil, and Duroliopaque is desirable to determine the contrast medium best

suited for sialography. In that clinical study, glandular overfilling should be avoided and special attention should be given to the radiopacity of the media after dilution, the evacuation of the media from the salivary glands, subjective side effects, and the quality of the sialograms.

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Appendix

Composition of artificial saliva used in this study⁵⁰:

Na-carboxymethylcellulose medium	
viscous	10 g/l

Sorbitol	30
KCl	1.2
NaCl	0.855
MgCl ₂ · 6H ₂ O	0.050
CaCl ₂ · 2H ₂ O	0.218
K ₂ HPO ₄	0.343
Methylparaben	1
Aqua ad 1,000 ml	

During the progression of the *in vitro* experiments a second type of artificial saliva* became available. The most important difference from the above-

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mentioned artificial saliva is the replacement of the viscosity factor Na-carboxymethylcellulose medium viscous by mucin. Testing of some of the water-soluble media with this saliva resulted in slightly different values for dilution and evacuation *in vitro*.

Manufacturers of the investigated contrast media: Conray 80—Byk Gulden, Konstanz, West Germany. Isopaque 440, Amipaque—Nyegaard, Oslo, Norway. Urombrine 420—Dagra, Diemen/Brussels/Lisbon/Madrid. Urografin 76%, Endografin Schering, Berlin/Bergkamen, Germany. Hytrast, Lipiodol UF, Duroliopaque—Guerbet, Aulnay-sous-Bois, France. Dionosil oily, Myodil—Glaxo, Greenford, England.