# COMPLICATIONS IN DIAGNOSTIC RADIOLOGY

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EDITED BY

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# PREFACE

In recent years there have been spectacular advances in radiology. As in all other spheres of medicine, however, the increased benefit to the patient in diagnostic accuracy must be balanced against the inevitable small but significant risk of complications which may ensue. Because of the rarity of many of these complications, an individual radiologist will fortunately witness few of them during his career. Nevertheless, every radiologist must be conversant with these possibilities so that if a complication does arise, he will be able to diagnose this promptly and institute appropriate treatment. This book provides a comprehensive and authoritative review of the subject. Particular emphasis has been placed on techniques and fundamental principles, thereby providing a rational approach to prevention and treatment.

I am grateful to my colleagues, all acknowledged experts in their fields, who so readily agreed to contribute to the book. Radiologists will mourn the sad loss of Professor Arne Engeset and the chapter written in collaboration with Professor Lundervold will be a lasting tribute to his memory.

I should also like to thank the many radiologists who participated in the U.K. National Radiological Survey for the valuable information derived from their reports. Much of this material has been incorporated into the book where it provides an important and easily accessible source of reference.

Finally, I should like to pay tribute to the publishers for their helpful co-operation and for the excellent reproduction of the illustrations.

*June* 1976

GEORGE ANSELL

# CONTENTS

# CHAPTER 1. CONTRAST MEDIA IN UROGRAPHY

G. ANSELL

## EXCRETION UROGRAPHY

In recent years, several major reviews of contrast media have been published [1–3]. The intravascular contrast media used for excretion urography and angiography are water-soluble derivatives of organic acids and their radio-opacity is directly related to their iodine content. The di-iodinated pyridine derivatives iodomethamate (iodoxyl) and iodopyracet (diodone) are now largely of historical interest. Modern tri-iodinated compounds are derivatives of benzoic acids. The earliest of these, acetrizoate (Diaginol, Urokon) has now been superseded for intravascular use in the United States, United Kingdom and Scandinavia because of its relative toxicity but it is still used in some other countries. The main tri-iodinated benzoic acid derivatives in current use are diatrizoate (Hypaque, Urografin, Renografin), iothalamate (Conray), metrizoate (Isopaque, Triosil) and iodamide (Uromiro).

In terms of toxicity on an equiosmolar basis, there is little difference between these anions. However, in certain specific circumstances, the methylglucamine cation decreases local endothelial toxicity. This is mainly of value in the cerebral and coronary circulations and for peripheral arteriography. For excretion urography, the evidence now tends to favour the use of pure sodium media since methylglucamine may indeed have certain disadvantages which are discussed in later sections of this chapter. Commercial preparations contain varying combinations of sodium and methylglucamine salts. This can result in some confusion when comparisons are made between individual media. In addition, these media usually contain very small amounts of sodium citrate as a buffer, and salts of the chelating agent ethylenediaminetetracetic acid (EDTA) to stabilize the solution.

If large doses of contrast media are administered to animals to determine the $LD_{50}$, a characteristic syndrome occurs [4]. As lethal dose levels are

approached, the animals become apprehensive; vomiting (except in rodents), urination and defaecation occur, followed by muscle twitchings and convulsions. At a later stage, capillary breakdown develops in the lungs causing pulmonary haemorrhage and right heart failure. The $LD_{50}$, i.e. the dose causing the death of 50 per cent of the animals, is mainly of value in comparing the toxicity of different contrast media but it does not give a direct indication of the *safe* dose for clinical use in man. In any large population sample, a dose–response curve would indicate that a few individuals would be unduly susceptible to a dose which is safe for the majority. At the other extreme of the curve, a few individuals would tolerate an even larger dose than the majority.

In clinical use, the manifestations of contrast media reactions will depend partly on the dose involved and partly on the manner in which it is administered. They can be considered under three main categories:

1 Idiosyncrasy reactions in a susceptible patient from a dose of contrast medium which would be harmless to most patients. These reactions were originally considered to be allergic, but despite a voluminous literature on the subject, their aetiology is still poorly understood and there are probably several different factors involved in this group.

2 Reactions following the use of a large total dose of contrast medium in high-dose urography, angiography or, occasionally, as a result of accidental overdose.

3 Reactions occurring when a concentrated bolus of contrast medium has been delivered to a critical area such as the myocardium, brain, spinal cord or kidneys.

The reactions in the last two categories depend largely on the known chemotoxic effects of contrast media and on their hypertonicity. This chapter deals primarily with the general effects of contrast media. The specific effects, occurring as a result of their use in specialized procedures, are considered in the corresponding chapters.

## IDIOSYNCRASY REACTIONS

### *Classification and incidence*

Since the aetiology is unknown, any classification of idosyncrasy reactions must be arbitrary but a practical classification can be based on the severity of the reaction as it involves the general condition of the patient and the necessity for treatment. In the U.K. National Survey which was based on more than 300 000 urographic examinations [5], the following classification was therefore used (Table 1.1).

1 Minor reactions

Those which usually required no treatment.

2 Intermediate reactions

These usually required some form of treatment but there was no undue alarm for the patient's safety, and the response to treatment was usually rapid.

TABLE 1.1. Classification of reactions [5].

| Minor | Intermediate | Severe |
|---|---|---|
| Nausea, retching | Faintness | Severe collapse |
| Slight vomiting | Severe vomiting | Loss of consciousness |
| Feeling of heat | Extensive urticaria | Pulmonary oedema |
| Limited urticaria | Oedema of face or glottis | 'Cardiac arrest' |
| Mild pallor or sweating | Bronchospasm | Myocardial infarction syndrome |
| | Dyspnoea | Cardiac arrhythmias |
| Itchy skin rashes | Rigors | |
| Arm pain | Chest pain | |
| Sneezing | Abdominal pain | |
| | Headache | |

3 Severe reactions

There was often fear for the patient's life and intensive treatment was required in most cases.

4 Death

In the survey, a considerable number of reactions were classified as 'minor' but, since the reporting of this type of reaction in a heterogeneous survey was likely to be variable, no attempt was made to compute their incidence. In a study at the Ochsner Clinic involving 40 000 urograms [6], the incidence of 'mild' reactions was 8 per cent and, in a Mayo Clinic series involving approximately 30 000 patients [7] the incidence of 'minor' reactions was 5.1 per cent. However, most patients in the Mayo Clinic series suffered from trivial

symptoms such as mild hot flush, metallic taste in the mouth, mild nausea, cough, sneezing, tingling of the skin, etc. Similar 'trivial' symptoms were reported in 59 per cent of urograms, in a smaller recent investigation [8], and they appeared to be related to the dose and to speed of injection. Among the trivial symptoms reported in this study were unpleasant perineal sensations such as burning, a feeling of wetness, or a desire to empty the rectum or bladder, sometimes accompanied by a spurious sensation of having done so. These latter sensations apparently occurred in nearly 40 per cent of cases [8].

The incidence of intermediate reactions, severe reactions and death in the U.K. survey are shown in Table 1.2. It is difficult to compare these with other series in the literature due to differences in classification. In the Mayo Clinic series [7], the incidence of 'moderate' reactions was 1 in 112 and of

TABLE 1.2. Incidence of reactions in 318 500 excretion urograms. U.K. National Survey 1966–69 [5].

| | Intermediate reactions | Severe reactions | Death |
|---|---|---|---|
| Reports received | 142 | 24 | 8 |
| Incidence | 1 in 2000 (0.05%) | 1 in 14 000 (0.007%) | 1 in 40 000 (0.0025%) |

'severe' reactions 1 in 1100, but only about one-third of this severe group appeared to be 'life-threatening' giving an incidence of 1 in 3000 to compare with the incidence of 1 in 14 000 found in the U.K. survey. In a survey of 12 419 paediatric patients, the overall incidence of reactions noted was 3.4 per cent and the incidence of severe reactions was 1 in 2500 [9].

In the classical North American survey during the years 1942 to 1958, Pendergrass *et al.* [10] found a mortality rate of 8.6 per million urograms (1 in 117 000). In France between the years 1955 and 1965, Wolfromm [11] found an incidence of approximately 1 in 61 000, and from Italy, Toniolo [12] reported a mortality rate of 1 in 85 000. It was widely believed that with the reduced toxicity of currently used contrast media, the mortality rate would improve. However, this has not in fact occurred. The mortality in the U.K. survey was 1 in 40 000, and this has since been confirmed by a recent survey in the U.S. where Fischer [13] found a mortality rate of 1 in 50 000.

TABLE 1.3. Urographic reactions related to age [5].

| Age (years) | Unkn. | 0–9 | 10–19 | 20–29 | 30–39 | 40–49 | 50–59 | 60–69 | 70+ | Under 50 | Over 50 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Intermediate reactions (Total = 164) | 17 | 4 | 10 | 20 | 26 | 32 | 21 | 27 | 7 | 92 | 55 |
| Severe reactions (Total = 43) | 8 | | 1 | 3 | 5 | 8 | 5 | 5 | 8 | 17 | 18 |
| Deaths U.K. survey (Total = 13) | | 2* | | | | | 6 | 2 | 3 | 2 | 11 |
| Deaths Pendergrass [10] (Total = 61) | 3 | 3 | | 4 | 5 | 7 | 10 | 12 | 17 | 19 | 39 |

* Overdosage.

This table also includes a number of cases reported to the U.K. survey prior to 1966 which were not used in computing the incidence rates shown in Table 1.2.

Indeed, these rates might have been higher, had it not been for the use of modern methods of resuscitation which would not have been available at the time of the earlier surveys. It seems possible, therefore, that the relative increase in mortality, as compared with the earlier surveys, may be due to the less restrictive selection of patients for urography and possibly also to the higher dosage schedules currently in use. Shehadi's most recent figures suggest a mortality rate as high as 1 in 13 000 urograms [14].

There does not appear to be any sex difference in the incidence of reactions but data derived from the U.K. survey suggests that age has a significant effect on the severity of the reactions sustained (Table 1.3) [5]. If it is assumed that the more numerous intermediate reactions are broadly representative of the age distribution of urographic examinations, then there appears to be a progressive spectrum of increasing severity of reactions with advancing age. This is more easily seen if an arbitrary dividing line is taken at the age of 50. Intermediate reactions are more frequent below this age; severe reactions show a higher age-peak with equal numbers occurring below and above the age of 50; whilst the majority of deaths occur in the older age groups. Data from Pendergrass' paper [10] have also been analysed in a similar manner and are given in Table 1.3. Although these show a wider scatter, deaths again predominate in older patients. These findings suggest that when a reaction occurs in an older patient, there may be an impaired ability of the cardiovascular system to respond to the insult. These findings in the U.K. survey are in contradistinction to those of an earlier much quoted study [15] which showed a lower incidence of side effects in the elderly as compared with younger adults, but this related mainly to minor reactions.

## CLINICAL CHARACTERISTICS IN NONFATAL REACTIONS

Reactions are unpredictable and usually occur either during the injection or within the following five to ten minutes. However, occasionally, they may be delayed in onset. Symptoms of the minor reactions have already been discussed briefly. Table 1.4 shows the relative frequency of the various clinical features of intermediate and severe reactions in the U.K. survey [5]. In the individual cases, there was often more than one basic feature and these are each counted separately so that the numbers of 'symptoms' exceeds the numbers of patients with reactions.

### *Mucocutaneous lesions*

Under this heading are included reactions involving the skin or mucous

membranes, such as erythema, rashes, urticaria or angioneurotic oedema. This group most resembles the symptoms which might be expected if an allergic reaction or histamine release were a significant factor. These lesions occurred in more than one-third of the intermediate reactions but in only one-sixth of the severe reactions. Sneezing is another occasional symptom

TABLE 1.4. Clinical analysis of intermediate and severe reactions following excretion urography.

| | Intermediate reactions (164 patients) | Severe reactions (43 patients) |
|---|---|---|
| Mucocutaneous | 66 (40.2%) | 7 (16.3%) |
| Hypotension | 46 (28.0%) | 35 (81.4%) |
| Bronchospasm | 23 (14.0%) | 5 (11.6%) |
| Myocardial | 0 | 12 (27.9%) |
| Vomiting | 20 (12.2%) | 5 (11.6%) |
| Rigors | 29 (17.7%) | 2 (4.7%) |
| Headache | 14 (8.5%) | 0 |
| Abdominal pain | 8 (4.9%) | 2 (4.7%) |
| Pain in chest | 7 (4.3%) | 1 (2.3%) |
| Convulsions | 3 (1.8%) | 4 (9.3%) |
| Sneezing | 4 (2.4%) | 4 (9.3%) |
| Paraesthesiae | 7 (4.3%) | 0 |

Many reactions had more than one clinical feature so that the totals for 'Symptoms' exceed the totals for the numbers of 'Reactions'.

Percentage figures indicate *comparative* frequency of symptoms in intermediate and severe reactions only. Incidence rates for reactions are shown in Table 1.2.

suggesting an allergic or histamine-like reaction. It is usually of only minor inconvenience but it may rarely presage a severe or even fatal reaction. In one patient, marked oedema of the face persisted for three days. In another patient, oedema of the face was associated with blurring of vision. Rarely, there may be delayed skin rashes and severe toxic eruptions have occurred up to two weeks after urography.

*Bronchospasm*

Asthmatic patients appear to form an unduly susceptible group. Severe bronchospasm sometimes occurred with cyanosis, and in one patient the asthmatic attack progressed to cardiac arrest which was fortunately reversible. As little as 0.5–1 ml of contrast medium could provoke a serious attack and one-quarter of the patients received less than 10 ml. Methylglucamine contrast media appeared to be more likely to cause bronchospasm and this is discussed in a later section. Sixteen of the twenty-eight patients had a previous history of asthma and two had an alternative allergic history. However, skin rashes appeared to be uncommon in association with bronchospasm. Although there is an increased risk in asthmatic patients, only a small proportion actually develop an attack following urography. In the Mayo Clinic series [7], this occurred in 6 per cent of patients with a history of asthma.

*Vomiting*

This appeared to be a relatively nonspecific symptom but it could be distressing and occasionally it presaged a severe reaction. In one patient, inhalation of vomit lead to death. There appeared to be some evidence of a dose relationship. In the intermediate and severe reactions in the U.K. survey, the relative incidence of vomiting in infusion urograms was some seven times that noted with conventional doses. In one patient, the worst vomiting was delayed until 1½ hours after the infusion. Metoclopramide may be useful in the treatment of persistent vomiting [16].

*Hypotension*

Hypotensive collapse is one of the most important features of contrast media reactions. Hypotension occurred in about one-quarter of the intermediate reactions and in the majority of the severe reactions. In the latter group, it was usually profound, often associated with transitory loss of consciousness, and occasionally accompanied by incontinence. In the unconscious patient there is a major risk of airways obstruction by the tongue falling back, with resultant cyanosis. This requires immediate attention. The pulse in hypotensive collapse was sometimes rapid and thready whereas in other cases there was bradycardia. The skin was often cold and clammy and occasionally there was profuse perspiration. In the Mayo Clinic series [7] apparently all the cases of severe hypotension were associated with a diffuse erythematous

rash and preceded by nausea and vomiting. In the U.K. series [5] an erythematous rash was only reported infrequently in the severe cases of hypotensive collapse. The reason for this discrepancy is uncertain. The contrast medium used in the Mayo Clinic was 69 per cent sodium methylglucamine diatrizoate (Renovist). It may be a coincidence that in the few cases in the U.K. series where an erythematous rash was reported in hypotensive collapse, a number had received a similar medium (Urovison).

Syncope may also occur due to fear or nausea or it may occasionally result from decreased venous return to the heart as a result of inferior vena caval obstruction by abdominal compression.

Minor degrees of hypotension usually require no treatment but in severe cases, vigorous treatment is often required with vasopressors and steroids. Prolonged shock may also be associated with hypovolaemia and it may fail to respond to vasopressors until this has been corrected [17]. A syndrome resembling shock-lung with diffuse pulmonary infiltrates has also been described following a severe contrast medium reaction [18]. Hypotensive shock usually occurs within the first few minutes of the injection but may rarely be delayed. In two patients, hypotension developed approximately one hour after the examination [5]. In one patient, circulatory collapse with prolonged unconsciousness was followed, on recovery, by the passage of offensive blood-stained stools [19].

*Cardiac disorders*

Sudden cardiac arrest following the administration of contrast medium is the most dramatic of the severe reactions but, with external cardiac massage and resuscitation, there is a reasonable prognosis for full recovery. Arrhythmias may occur and there may be other transitory electrocardiographic changes. These changes are more likely to occur in older patients or in patients with a previous history of heart disease. In several cases they were initially attributed to myocardial infarction but review of the follow-up data showed that the ECG changes were nonspecific. Occasionally however, hypotensive collapse may be associated with unequivocal ECG evidence of coronary infarction and it may then sometimes be problematical whether the coronary infarction occurred incidentally, or whether it resulted from a hypotensive reaction to the contrast medium. It seems likely that in the majority of cases, ECG changes could be due to the direct toxic affect of the contrast medium on the myocardium [5]. Supporting evidence for this view has been provided by Berg *et al.* [20] who monitored electrocardiograms in ten patients undergoing excretion urography with 50 ml of 60 per cent methylglucamine diatri-