7.1 Introduction

Acute idiosyncratic systemic reactions (also described as allergy-like or anaphylactoid) are defined as unpredictable reactions that occur within 1 h of contrast medium administration, and are unrelated to the amount of contrast medium above a certain level. This definition aims to distinguish them from chemotoxic reactions, which are dose-related and dependent on the physico-chemical properties of the contrast medium. However, in clinical practice, some reactions such as cardiovascular collapse may be difficult to characterise definitely into one or the other group.

Most of this chapter is concerned with acute idiosyncratic reactions to iodinated contrast media, particularly the factors predisposing to these reactions and the measures that may be taken to prevent them. At the end of the chapter, acute reactions to gadolinium contrast media are also discussed (see also Chap. 23).

7.2 Iodinated Contrast Media

7.2.1 Types and Timing of Acute Reactions

Many patients who are given intravascular iodinated contrast media experience some subjective sensations such as warmth, flushing, and altered taste. These common effects usually last for a few minutes and are not of clinical significance.

In radiological literature, acute idiosyncratic reactions have been classified as mild or minor, moderate, or severe (Bush and Swanson 1991). Mild or minor
reactions usually do not need treatment and include nausea, mild vomiting, urticaria, and itching. Moderate reactions include more severe vomiting, marked urticaria, bronchospasm, facial or laryngeal oedema, and vasovagal reactions. Severe reactions include hypotensive shock, pulmonary oedema, respiratory arrest, cardiac arrest, and convulsions. While this type of classification is widely used in clinical practice, it has been suggested that Ring and Messmer’s four-grade classification of anaphylactic reactions would provide more detailed and reproducible documentation of acute reactions (Idee et al. 2005).

Most acute reactions occur early after contrast medium administration. In Katayama et al’s (1990) study of over 330,000 patients, over 70% of reactions to both ionic and nonionic contrast media occurred in the first 5 min. In all 44 patients who died after intravascular contrast medium (reviewed by Shehadi (1985)), the acute reaction to contrast medium started within 15 min of administration.

The general incidence of anaphylactic reactions is increasing (Resuscitation Council (UK) 2008). It is not known whether this is also the case for anaphylactoid reactions to contrast media.

7.2.2 Mechanisms of Acute Reactions

The mechanisms by which acute adverse reactions to iodinated contrast media occur are still unclear (Idee et al. 2005; Morcos 2005; Dewachter et al. 2006) and this makes prevention of reactions more difficult.

True allergic hypersensitivity appears to account for at least some severe acute reactions. Laroche et al. (1998) showed immediate marked rises in plasma histamine and tryptase levels in patients who had severe acute reactions, with the levels being proportional to the severity of the reaction. The timing and size of the increases were similar to those observed in known allergic hypersensitivity reactions, which suggested that immediate mast cell degranulation had occurred. Contrast-medium-specific IgE levels were higher in severe reactors than controls (Laroche et al. 1998). In some severe reactors, skin testing with contrast medium was positive (Laroche et al. 1998; Dewachter et al. 2006). Some cross-reactivity between contrast media has been shown in reactors, and in some patients non-cross-reacting contrast media were subsequently administered without problems (Dewachter et al. 2006).

How iodinated contrast media act as antigens remains a problem, as they bind poorly to protein (Lasser et al. 1962). One suggestion, based largely on in vitro experiments, is that contrast media act as “pseudoantigens” that attach to the fixed Fc site on the IgE molecule rather than the variable Fab site of specific antigen binding (Lasser 2004). Lasser has proposed that in low concentrations contrast media cause binding of adjacent IgE molecules leading to mast cell activation, and that, in higher concentrations, contrast media inhibit IgE binding because the aggregation of contrast medium molecules causes steric hindrance (Lasser 2004). Others have not been able to show the aggregation of contrast medium molecules, considered necessary for this effect (Sontum et al. 1998).

When mast cells are activated, heparin is also released and can activate the contact system with the release of bradykinin (Lasser 1987, 2004). In addition, other mediators, such as prostaglandins, leucotrienes, and cytokines, are likely to be involved (Dewachter et al. 2006).

Complement levels in the blood decrease after contrast medium, both in control subjects and reactors, with the decreases being greater in the reactors (Eloy et al. 1991). Although contrast media may be able to activate the complement system, it is considered unlikely that this mechanism is responsible for acute reactions (Dewachter et al. 2006).

The immediate non-allergic effects of contrast media could be caused by direct chemotoxicity. They could also relate to the non-specific release of small amounts of histamine from mast cells and/or basophils, which occurs in up to 80% of patients in the minutes immediately after contrast medium (Eloy et al. 1991; Rodriguez et al. 2001; Dewachter et al. 2006). This effect relates to the nature of the contrast medium molecule as well as the dose and osmolality of the contrast agent.

7.2.3 Risk Factors for Acute Idiosyncratic Reactions

7.2.3.1 Type of Contrast Agent

With the older high-osmolality ionic agents, the rate of reactions of all types is in the range 5–12% (Ansell et al. 1980; Witten et al. 1973; Shehadi 1975; Katayama et al. 1990; Cochran et al. 2001). Most reactions in these series were mild, with moderate