Effects on the Blood and Endothelium

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17.1 Introduction

Iodinated contrast media are widely used either to visualize blood vessels (angiography) or to enhance the density of the parenchyma of different organs. In both instances, they are administered intravascularly and ideally their effects on blood and endothelium should be minimal. However, all contrast media have some effects on the endothelium, blood, and its constituents. There is a vast literature on these effects both in vitro and in vivo. The present chapter summarizes the effects from a clinical perspective in order to clarify whether there are important differences between the types of iodinated contrast media in current clinical use.

Iodinated contrast media may be either ionic or nonionic and they all produce various effects on blood components. These effects are thought to be caused by the chemical nature of contrast media, their electrical charge, and by the viscosity and the osmolality of the solution in which they are given. Different contrast media have varying effects on the many components of the blood.

The hematologic effects of iodinated contrast media have been divided into the following categories: red blood cells, white blood cells, endothelium, platelets, coagulation, and fibrinolysis.

17.2 Red Blood Cells

The effect of contrast media on red blood cells can be divided into the effects on morphology, aggregation, and rheology (flow properties of the blood). When iodinated contrast media come into contact with red blood cells, the normal discoid shape of the red
blood cells changes (Aspelin et al. 1980; Nash and Meiselman 1991). Two changes caused by extraction of water may occur: either shrinkage of the red blood cells producing a dessicocyte, or changes in shape called echinocyte or stomatocyte deformation.

### 17.2.1 Red Cell Morphology

Dessicocyte formation is an in vitro effect of dehydration of the red blood cell and is proportional to the osmolality of the contrast media to which it is exposed (Aspelin et al. 1980). It is observed only in a fraction of red blood cells if exposed to almost undiluted high-osmolar contrast medium.

Echinocyte formation in vitro is dependent on the chemotoxicity (including electrical charge, pH, or salt concentration) (Chronos et al. 1993) and not on the osmolality of the contrast agent. All contrast media including the iso-osmolar dimers may induce some degree of echinocyte formation (Hardeman et al. 1991; Aspelin et al. 1987).

### 17.2.2 Red Blood Cell Aggregation

Contrast media in vitro cause disaggregation of red blood cell rouleaux and not aggregation as sometimes believed (Aspelin et al. 1987). The reason for the misunderstanding could be that contrast media make red cells more rigid causing precapillary stasis, which can be mistaken for increased red blood cell aggregation (Aspelin and Schmid-Schönbein 1978; Aspelin 1992).

### 17.2.3 Blood Rheology

The combined effect of the dessicocyte, echinocyte, and stomatocyte is reduced plasticity of the red blood cells as compared with normal red blood cells (Aspelin and Schmid-Schönbein 1978; Aspelin 1992; Losco et al. 2001). Plasticity is essential for the smooth flow of red blood cells through small capillaries and when it is lost there is a decrease in blood flow especially after intra-arterial injections (Dawson et al. 1983; Le Mignon et al. 1988; Strickland et al. 1992b; Pugh 1996). Pure echinocyte and stomato-

cyte formation without any dehydration of red blood cells produces only minor rheological change (Aspelin et al. 1980; Nash and Meiselman 1991). However, the overall in vivo effect is a mixture of the effect of contrast media on red blood cell morphology, rigidity, viscosity, and vascular tone. Contrast media can induce both vasoconstriction and vasodilatation in different organs (Morcos et al. 1998; Mills et al. 1980; Almén et al. 1980; Liss et al. 1996). In the pulmonary circulation, contrast media can induce red cell rigidity and pulmonary arterial vasoconstriction, leading to an increase in pulmonary vascular resistance (Pugh 1996; Morcos et al. 1998; Mills et al. 1980; Almén et al. 1980). In the kidney, contrast media can reduce the blood flow in the vasa recta in the medulla (Liss et al. 1996). It is not clear whether this effect is mainly caused by stasis due to vasoconstriction or by increased red blood cell aggregation in vivo. The morphological red cell changes may also affect the capacity for oxygen delivery and pH buffering (Galtung et al. 2002). However, these effects have not been proven to be of importance in clinical studies (Strickland et al. 1992a).

The overall effect of contrast media on red blood cells has not been shown to be of clinical importance.

### 17.3 White Blood Cells

The function of the white blood cells is mainly host defense, but their interactions with the endothelial cells and platelets are also important. White blood cells must be able to adhere to the endothelium and migrate through the vessel wall in order to phagocytize and inactivate toxic products. This involves adherence, chemotaxis, degranulation, and phagocytosis. In vitro studies have shown that all these processes are affected by contrast media.

#### 17.3.1 Phagocytosis

Contrast media reduce the ability of white blood cells to exhibit phagocytosis (Rasmussen et al. 1988, 1992b; Rasmussen 1998). This effect has been studied only with ionic, high-osmolar contrast media. It may also be caused by calcium chelating agents in the solution. The clinical importance of these in vitro observations is not known.