Leukocyte Depletion in Cardiac Surgery and Cardiology
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Editors

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32 figures and 15 tables, 2002
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The concept of leukocyte depletion by means of a leukocyte removal filter was introduced by Fleming in 1926 and was also proposed by Wright. During the past decades, leukocyte depletion has become an important tool for the prevention or reduction of the pathogenic effects (posttransfusion syndrome, virus infection/transmission) of blood transfusion. The reduced pathogenicity of leukocyte-depleted blood products significantly reduced the overall cost per patient transfused. Currently, an increasing number of countries recommend or make universal filtration of blood transfusions mandatory. While the filtration of all blood products is not yet mandatory in the US, the medical community, following the recommendations of the Blood Products Advisory Committee of the FDA, has been advising that all donor blood should be filtered to remove white cells. The American Red Cross has publicly stated its intention to reach this goal by the end of 2001. Routine filtration of all whole blood, red blood cells and platelets has become mandatory in Germany as of October 2001.

In cardiac surgery, where transfusion of blood products or perfusion is required, leukocyte depletion has evolved as an important tool. Patients receiving foreign leukocytes have to deal with the posttransfusion syndrome, transient immunosuppression, allogeneic immune reactions, and virus infections or (re)activation. Those who undergo cardiac surgery with cardiopulmonary bypass (CPB) and do not even receive foreign blood products may develop systemic inflammatory response and organ dysfunction mainly due to the activation of neutrophils.

The first specific leukocyte-depleting arterial line filter for CPB was introduced in 1991 and has subsequently been evaluated by several investigators (see...
the chapter by Palanzo, Allentown, Pa.). To date, several investigators have reported on the beneficial effects of leukocyte depletion in cardiac surgery regarding both clinical effects and cost reduction.

Despite the favorable results of leukocyte depletion in cardiac surgery with CPB, the exact mechanistic definition of the beneficial impact of leukocyte filters in limiting the pathogenicity of CPB remains quite elusive. To further advance leukocyte filter technology and filtration strategies, it is important to understand the complex biology of activated neutrophils and their role in cardiac surgery with or without CPB.

Neutrophil effector mechanisms represent major immune responses of the innate immune system. Independent of antigen presentation pathways via histocompatibility complexes I and II, neutrophils are activated after binding of their Fc receptors to immune complexes or of their complement receptors to central complement factors, such as C3a, C5a, C3b. Following activation, opsonized pathogens are eliminated via phagocytosis or exocytosis by lysosomal enzymes (e.g. muraminidase, myeloperoxidase, elastase) and oxygen radicals, mechanisms that may contribute to immunopathogenesis.

It is well established that CPB and the operation per se activate neutrophils via numerous pathogenic factors, such as contact with artificial surfaces of the extracorporeal circuit, and that activated neutrophils elicit severe endothelial injury by overshooting effector mechanisms. Neutrophil adhesion to and/or transmigration through the vascular endothelium are triggered by surface molecules, such as selectins and integrins, that allow firm adhesion to endothelial adhesion molecules. Complex intercellular mechanisms account for the subsequent neutrophil transendothelial migration, which involves disruption of interendothelial cell contacts (e.g. cadherins), enzymatic digestion of the extracellular matrices and consecutive formation of transient or persistent edema.

In the first chapter of this book, the biology of neutrophils and their pathogenic effects are considered by Gourlay et al. (London). This chapter demonstrates that leukocyte depletion is a logical strategy to limit neutrophil-mediated disorders in cardiac surgery. The cerebral sequelae of cardiac surgery with CPB are described by Scholz et al. (Frankfurt). The following chapter by Sheppard (Southampton) presents mechanisms and technical aspects of leukocyte depletion to limit the pathogenicity of activated leukocytes.

As the neutrophil-related pathomechanisms differ depending on the intervention (transfusion, transplantation, extracorporeal circulation, reperfusion), the strategies of leukocyte filtration have to be adapted to the particular clinical setting and will be discussed separately. The subsequent chapters cover transfusion (Henschler, Frankfurt) and transplantation (Scholz and Matheis, Frankfurt). The chapters on perfusion are introduced by a systematic study of filtration modalities (Matheis and Scholz, Frankfurt), followed by an introduction to
reperfusion injury during CPB by Krishnadasan et al. (Seattle, Wash.). Gu et al. (Groningen), Palanzo (Allentown, Pa.) and Matheis et al. (Frankfurt) report clinical studies with different objectives in adults. Allen analyzes some of the few studies available on CPB and leukocyte filters in infants. The chapter by Martin (Freiburg) deals with leukocyte filtration of blood cardioplegia. In the last chapter, Berg et al. (Frankfurt) speculate about future filtration strategies, such as bioactive cytokine filters.

In contrast with transfusion medicine, leukocyte filtration in cardiac surgery has not yet become a standard procedure despite the broad documentation of its beneficial effects. This may change when current studies on leukocyte filtration in cardiac surgery become available to a broader audience of practising surgeons and perfusionists.

This book reviews the experience with experimental and clinical leukocyte filtration, summarizes the state of the art in clinical application, and provides an outlook on the possible future role of leukocyte depletion in cardiology and cardiac surgery.

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