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On November 10 and 11, 1989 an international group of investigators convened in St Paul-de-Vence, France, for a workshop to consider newer aspects of the interactions of pentoxifylline and its analogs on leukocyte function. The first workshop took place two years earlier in Key Biscayne, Florida and at that time it became evident that there were a number of fascinating interactions of pentoxifylline with cytokines and leukocytes. Investigators at the first workshop developed the theme that inflammatory cytokines activate neutrophils and pentoxifylline and its derivatives can inhibit this interaction. In addition pentoxifylline decreases the production of tumor necrosis factor by stimulated macrophages. Workers went on to show that pentoxifylline was effective in reducing morbidity and mortality in several animal models of infection and inflammation. Many questions remained and investigators went back to their laboratories enthusiastic, but puzzled by some of the results.

The present workshop attempts to further clarify the mechanisms of action, the effects and the clinical potential of the interaction of pentoxifylline and leukocytes. The first part of the symposium examines in vitro studies, focusing on the mechanisms of pentoxifylline action on leukocytes. Parameters studied include Chemotaxis, oxidative activity, adhesive properties, interaction with endothelium and the generation of thrombi. The data generated supports the concept that pentoxifylline and its analogs had an anti-inflammatory effect and decreased oxidative capacity, adherence and endothelial interactions of leukocytes. Further studies looked at the fine structural effects of pentoxifylline in leukocytes, examining the actin state, receptor expression and membrane fluidity of the cells. It was again noted that pentoxifylline seemed to counteract the adverse effects of neutrophil activation. Preclinical studies examined the activity of pentoxifylline and related agents in animal models of sepsis, peritonitis,
hemorrhagic shock, lung injury, endotoxic shock, surgical adhesion and vascular injury. The results generally supported a protective activity of pentoxifylline in these states.

Finally, the results of preliminary clinical studies were reported, looking at such diverse situations as ARDS, multi-organ failure, asthma, cardiopulmonary bypass, head and neck surgery, radiation injury and hemodialysis. The studies strongly suggested that in many of these conditions pentoxifylline appeared to be beneficial. However, since the studies were preliminary, they only serve to reinforce the need for carefully done placebo-controlled blinded studies in selected conditions.

Analysis of the papers from this workshop should allow investigators to select those conditions that would most likely benefit from the unique actions of pentoxifylline and its analogs. Once these conditions are identified, clinical investigators working hand in hand with basic scientists should further clarify the role of these agents in our therapeutic armamentarium.