The potential role of ANCAs and cytokines in neutrophil-mediated vascular injury

**Figure 2. The potential role of ANCAs and cytokines in neutrophil-mediated vascular injury.** (a) Neutrophil and endothelial cell activation. Infection or other inflammatory stimuli lead to the production of pro-inflammatory cytokines [e.g. interleukin 1 (IL-1), tumour necrosis factor (TNF)], which induce resting neutrophils to express proteinase 3 (Pr3) and myeloperoxidase (MPO) on their cell surface. IL-1 and TNF also induce neutrophils and endothelial cells to increase their expression of adhesion molecules. (b) ANCA-induced neutrophil degranulation and vascular injury. The increased expression of adhesion molecules leads to binding of activated neutrophils to the vascular endothelium. Circulating ANCAs (anti-neutrophil cytoplasmic antibodies) bind to membrane-associated Pr3 or MPO and the FcγRIIa receptor, inducing neutrophil degranulation and generation of oxygen radicals, which results in endothelial cell injury and inflammation. Activation of neutrophils by ANCAs also results in release of inflammatory mediators such as IL-1 and IL-8, and bioactive lipids such as leukotriene B4. Figure based on illustration published in Ref. 94. ANCA, anti-neutrophil cytoplasmic antibody.