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NITRIC OXIDE AS A NATURAL ANTITHROMBOTIC AGENT

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Nitric oxide (NO) displays a number of biologic effects relevant to the prevention of thrombosis, such as vasodilatation, inhibition of platelet adhesion and aggregation, prevention of smooth muscle cell proliferation. Within the cardiovascular system, NO is mainly produced by endothelium but circulating blood cells, including platelets, may contribute to its production. Elevated shear stress at sites of arterial stenosis is a powerful platelet-activating stimulus but it also activates the production of NO by endothelium. Platelets contain constitutive NO synthase and several agonists can activate production of NO by platelets. We carried out a series of experiments to clarify the role of platelet-derived NO in the defence against thrombosis. We have shown that high shear stress induces the release of NO by platelets and that platelet-released NO limits shear stress-induced activation. We have also demonstrated that endogenous NO inhibits platelet-dependent thrombosis and favours platelet disaggregation in the mouse and rabbit. Finally, evidence is accumulating that defective platelet production of and/or sensitivity to NO accompanies some clinical conditions associated with arterial thrombosis, such as smoking, diabetes, acute coronary syndromes. Hyperhomocysteinemia is emerging as an important risk factor for thrombosis. We have assessed the effect of a methionine load on platelet NO production in 22 subjects at risk of thrombosis. NO production by ADP- or Collagen-stimulated platelets was strikingly decreased after methionine load and this was paralleled by a significant increase of ADP, Collagen- or shear stress- induced activation. In conclusion, platelet-released NO may act as a natural antithrombotic agent.