Nitric oxide (NO) produced by endothelial cells interacts with erythrocyte through protein band 3, being scavenged by haemoglobin. A signal transduction mechanism involving protein Gi and protein band 3 stimulates erythrocyte NO efflux when acetylcholine (ACh) binds to erythrocyte membrane acetylcholinesterase. Binding of fibrinogen (Fib), to erythrocyte membrane CD47 decreases the NO efflux. When high Fib concentration and ACh were present the efflux of NO from erythrocytes was compromised. The increased NO efflux from erythrocytes in presence of high Fib concentration and band 3 phosphorylation is reinforced in the presence of 4N1K an agonist peptide of CD47. When both Fib and 4N1K are present the NO efflux from erythrocytes is higher or not affected according lower or high levels of cAMP. Erythrocyte NO efflux in patients with systemic lupus erythematosus and rheumatoid arthritis was significantly negative associated with carotid intima-media thickness. In patients with amyotrophic lateral sclerosis erythrocyte NO content is preserved and an inverse association between respiratory function and NO efflux from the erythrocyte was verified. Sepsis patients before dead at 24h showed higher efflux of NO from erythrocytes that worsening the blood sub lingual microcirculation observed by high unequal blood flow and high microvascular flow index. The in vivo animal models either of inflammation or of hypertension evidenced that the NO efflux from erythrocyte decrease.