

**Andreoli S. Mechanisms of endothelial cell ATP depletion after oxidant injury. *Pediatric Res* 1989;25(1):97-100**

To investigate mechanisms of ATP depletion in human umbilical vein endothelial cells after oxidant injury, we studied the relationship between DNA damage, activation of the DNA-repairing enzyme poly ADP-ribose polymerase, NAD depletion, and ATP depletion. We found that oxidant stress generated with hypoxanthine-xanthine oxidase and glucose-glucose oxidase resulted in profound DNA damage. When endothelial cells were exposed to 25 and 50 mU/ml xanthine oxidase for 60 min, the percentage of double-stranded DNA was significantly reduced ( $p$  less than 0.05) to 15.2  $\pm$  1.2 and 4.6  $\pm$  0.5%, respectively, compared to 75.7  $\pm$  3.9% for control cells. When endothelial cells were exposed to 25 and 50 mU/ml glucose oxidase for 60 min, the percentage of double-stranded DNA was significantly ( $p$  less than 0.05) reduced to 35.0  $\pm$  1.5% and 9.9  $\pm$  7.7%, respectively, compared to 73.2  $\pm$  2.4% for control cells. ATP and NAD levels declined simultaneously with DNA damage. Because activation of the DNA-repairing enzyme poly ADP-ribose polymerase can consume NAD sufficient to interfere with ATP synthesis, we studied NAD and ATP levels after oxidant injury when ADP-ribose polymerase was inhibited with 3-aminobenzamide and nicotinamide. When poly ADP-ribose polymerase was inhibited, NAD levels remained normal, but ATP depletion was not prevented. We conclude that oxidant injury to human umbilical vein endothelial cells results in profound DNA damage and NAD and ATP depletion. NAD depletion results from activation of poly ADP-ribose polymerase, but this phenomenon is not the mechanism of ATP depletion in human umbilical vein endothelial cells.