

## Effect of Arsenic on Acetylcholine-Induced Relaxation in Blood Vessels *in vitro* and *in vivo*

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Several epidemiological studies suggested that arsenic exposure was strongly correlated with the development of cardiovascular disease such as hypertension. In order to examine whether arsenic affects vasomotor tone in blood vessels, we investigated the effect of arsenic on agonist-induced vasorelaxation using the isolated rat aortic rings in *in vitro* organ bath system. Treatment with arsenite inhibited acetylcholine-induced relaxation of aortic rings in a concentration-dependent manner. The inhibitory effects by arsenic were also observed in the relaxation induced by sodium nitroprusside, a NO-donor. Consistent with these findings, the cGMP levels stimulated by acetylcholine in blood vessels were reduced significantly by arsenite treatment. In addition, higher concentration of arsenite decreased the relaxation by 8-Br-cGMP, a cGMP analog, in aortic rings without endothelium. These *in vitro* results indicated that arsenite was capable of suppressing acetylcholine-induced relaxation in blood vessels by inhibiting production of nitric oxide in endothelial cells and by impairing the relaxation machinery in smooth muscle cells. *In vivo* studies revealed that the reduction of blood pressure by acetylcholine infusion was significantly suppressed after arsenite was administered intravenously to rats. These data suggest that vasomotor tone impaired by arsenite exposure may be one of the contributing factors in development of cardiovascular disease.