

# Whole-body hypoxic preconditioning protects mice against acute hypoxia by improving lung function

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Survival in severe hypoxia such as occurs in high altitude requires previous acclimatization, which is acquired over a period of days to weeks. It was unknown whether intrinsic mechanisms existed that could be rapidly induced and could exert immediate protection on unacclimatized individuals against acute hypoxia. We found that mice pretreated with whole-body hypoxic preconditioning (WHPC, 6 cycles of 10-min hypoxia-10-min normoxia) survived significantly longer than control animals when exposed to lethal hypoxia (5% O<sub>2</sub>, survival time of 33.2 ± 6.1 min vs. controls at 13.8 ± 1.2 min, n = 10, P < 0.005). This protective mechanism became operative shortly after WHPC and remained effective for at least 8 h. Accordingly, mice subjected to WHPC demonstrated improved gas exchange when exposed to sublethal hypoxia (7% O<sub>2</sub>, arterial blood PO<sub>2</sub> of 49.9 ± 4.2 vs. controls at 39.7 ± 3.6 Torr, n = 6, P < 0.05), reduced formation of pulmonary edema (increase in lung water of 0.491 ± 0.111 vs. controls at 0.894 ± 0.113 mg/mg dry tissue, n = 10, P < 0.02), and decreased pulmonary vascular permeability (lung lavage albumin of 7.63 ± 0.63 vs. controls at 18.24 ± 3.39 mg/dl, n = 6–10, P < 0.025). In addition, the severity of cerebral edema caused by exposure to sublethal hypoxia was also reduced after WHPC (increase in brain water of 0.254 ± 0.052 vs. controls at 0.491 ± 0.034 mg/mg dry tissue, n = 10, P < 0.01). Thus WHPC protects unacclimatized mice against acute and otherwise lethal hypoxia, and this protection involves preservation of vital organ functions.