

Environmental hypoxia during perinatal life enhances erythropoiesis and pulmonary vascular dysfunction in response to chronic hypoxia during adulthood: lessons from a murine model. W Mundo (MDc, MPH)¹, G Wolfson², D Park², CG Julian²

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Chronic hypoxia contributes to the development of cardiopulmonary disease at high-altitude (HA) residence and the factors influencing susceptibility are not well understood. Previous studies demonstrate that young HA males with pulmonary dysfunction were 6-times more likely to have experienced hypoxia during perinatal life, however the data did not allow fully account for the effect of unknown environmental exposures between gestation and adulthood. An experimental murine model in which the degree and timing of environmental hypoxia could be strictly controlled was used to assess the impact of perinatal hypoxia on pulmonary function and the development of polycythemia. Hypoxic exposure during adulthood increased RVSP by 79 % (25.2 vs. 45.2 mmHg, $p < 0.0001$), raised hematocrit by 34 % (40.2% vs. 53.8%, $p < 0.0001$), enhanced RV:LV+septum weight ratio 15 % (0.24 vs. 0.27, $p < 0.05$), reduced PAAT 15% (18.32 vs. 15.93, $p < 0.001$), and increased the magnitude of pulmonary vascular dysfunction and polycythemia in response to a secondary hypoxic exposure during adulthood in male offspring only. Perinatal hypoxia exaggerated the hypoxia-associated reduction of PAAT (15.9 vs. 12.8, $p < 0.0001$) and PV peak flow velocity (765 vs. 886, $p < 0.001$) and enhanced the hypoxia-associated increase of RVAW thickness (0.91 vs. 0.69, $p < 0.0001$) and hematocrit (57.7% vs. 53.8%, $p < 0.001$). This study highlights that perinatal hypoxia alone can induce lasting effects on pulmonary vascular function even in the absence of a secondary hypoxic exposure during adulthood. This study demonstrates that perinatal hypoxia increases the susceptibility to polycythemia and pulmonary dysfunction in early adult life in hypoxic and normoxic conditions.