OBJECTIVE: The objective of the study was to determine alterations in cGMP, soluble guanylate cyclase (sGC), phosphodiesterase type 5 (PDE5), and B-type natriuretic peptide (BNP), in an animal model of a congenital cardiac defect with increased pulmonary blood flow. 

DESIGN: Prospective, comparative, experimental study. 

SUBJECTS: Lambs, from birth until 8 weeks of age. 

METHODOLOGY: Late gestation fetal lambs underwent in utero placement of an 8 mm aortopulmonary vascular graft (shunt). In shunted and normal age-matched control lambs, at 2, 4, and 8 weeks of age, cGMP and BNP levels were measured, and sGC subunit and PDE5 protein expression were determined by Western blot analysis and immunohistochemistry. 

RESULTS: In shunted lambs, tissue and plasma cGMP levels were greater than normal throughout the 8-week study period (P< 0.05). sGCalpha protein was greater at 2 and 4 weeks (P< 0.05), and sGCbeta and PDE5 protein were greater at 4 weeks in shunted lambs (P< 0.05). Plasma BNP levels did not change in normal lambs but increased in shunted lambs by 8 weeks of age (P< 0.05). BNP levels were greater in shunted lambs than normal at 4 and 8 weeks (P< 0.05). 

CONCLUSIONS: Alterations in sGC subunit protein expression during the first post-natal month, and increased
BNP levels during the second post-natal month contribute to elevations in plasma and lung tissue cGMP in lambs with increased pulmonary blood flow.