

**Title:** CREATION OF PREGNANCY INDUCED HYPERTENSION MODEL IN THE PREGNANT EWE

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**Introduction.** Pregnancy induced hypertension (PIH) has eluded efforts to delineate its origins. The lack of an analogous animal model has delayed medical research efforts to date.

**Methods.** After approval by the animal care committee, four sheep were allowed to acclimatize for one week in the vivarium. One non pregnant ewe served as control while three pregnant ewes (# 1, 2, 3) with singleton fetuses at 65 days' gestation served as study animals. A low protein hay diet and water were available to all animals ad lib. Each week thereafter, following an overnight fast, the animals were anesthetized with halothane, nitrous oxide and oxygen and ventilation was controlled with a Bird anesthesia ventilator to maintain normal PaCO<sub>2</sub>. A foreleg vein was cannulated and lactated Ringer's infused at 200cc/hr. A 16g catheter was placed percutaneously into femoral artery and connected to a calibrated Gould transducer. Arterial blood pressure and ECG were recorded. Approximately 450-500cc blood was drawn from the arterial catheter into a closed blood collection system. The plasma was separated. The cells were suspended in saline (3cc saline: 1cc blood) and reinfused. Blood samples were analyzed for colloid osmotic pressure (COP), sodium, potassium, chloride, CO<sub>2</sub>, calcium, total protein, albumin, BUN, creatinine, glucose. After reinfusion of the suspended red blood cells the ewe was allowed to recover.

**Results.** No significant changes were seen in serum sodium, potassium, chloride, CO<sub>2</sub> or calcium. Two animals demonstrated rising BUN's. COP did not decrease until twice weekly plasmapheresis was begun. The control animals' COP ranged between 15 and 20mmHg while study animal's dropped to a low of 11-12 mmHg. After 10 plasmapheresis, ewe #1 developed a peak blood pressure of 150/90 with COP of 12.3 mmHg at 133 days gestation. Ewe #2 developed a peak blood pressure of 170/105 with a COP of 12.7 mmHg at 119 days gestation following 5 plasmapheresis.

Ewe #3 developed a peak blood pressure of 180/10 with a COP of 11.8 mmHg at 133 days gestation after 10 plasmapheresis. The control animal reached a peak blood pressure of 104/57 with a low COP of 17 mmHg after 8 plasmapheresis. Ewes # 1 and 3, delivered prematurely. Ewe #2 collapsed at 119 days gestation. Fluid resuscitation was successful for 2 days after which the ewe died.

**Discussion.** In 1973, Gant described a group of patients who had increasing sensitivity to angiotensin II at 18 week gestation and subsequently developed PIH.<sup>1</sup> Compared with the PIH group the normals lack of response to angiotensin resembled the normal blood volume expansion curve of pregnancy. Baker reported that COP fell below 19 mmHg before PIH developed.<sup>2</sup> Previous attempts to use the pregnant ewe as a PIH model have used exogenous catecholamines, renal artery banding, stress of herd separation and acute complete fasting to develop maternal hypertension.<sup>3,4</sup> This preliminary study suggests that depletion of albumin can lower colloid osmotic pressure resulting in what appears to be a physiologic model simulating human pregnancy induced hypertension.

**References.**

1. Gant N, Baley G, Chand S, et al: A study of angiotensin to pressor responses throughout primagravida pregnancy. *J Clin Invest.* 1973:52, 2682.
2. Baker E, Johnson J, Joyce TH: A redefinition of preeclampsia-eclampsia. SOAP abstract, 1982:40.
3. Khoury A, Wasserstrum N, Rudelsdorfer R, et al: Experimental hypertension in pregnancy, III. Central hemodynamic alterations in the kidney model. *Am J Obstet Gynecol* 1986:155:1231-1236.
4. Thatcher D, Keith J: Pregnancy induced hypertension: Development of a model in the pregnant ewe. *Am J Obstet Gynecol.* 1986:153, 201-107.