

therefore it was possible to distinguish retrospectively groups I and II in 10- and 14-day-old animals as well. At ages 10 and 14 days group I had a mean urine osmolality of 591.0 ± 17.4 mosmol/l and 610.9 ± 23.1 mosmol/l, group II 562.4 ± 26.4 mosmol/l and 583.9 ± 21.3 mosmol/l respectively. Hence the difference in concentrating ability becomes manifest in DI and non-DI rats at ages 18 days, and in adult-hood it further increases (584.0 ± 22.4 mosmol/l in homozygous and 2068.0 ± 134.4 mosmol/l in heterozygous).

Measurement of water intake (Figure 2) showed that, in individuals with a high urinary osmotic pressure, the water intake did not exceed 25 ml/100 g b.wt./24 h. Animals with low osmolality had a high water intake. In DI rats, there is a very tight distribution of values of

urinary osmotic pressure with a large scatter in values of water intake, whereas in non-DI rats the reverse is true. A similar non-linear relationship between water intake and urinary osmotic pressure was also observed in DI rats by VALTIN and SCHROEDER¹².

Hence, the concentrating ability of homozygous Brattleboro rats aged 10, 14 and 18 days does not differ from that of adult ones. The difference between homo- and heterozygous animals appeared at the 18th day of life, when the concentrating ability of the heterozygous increased significantly in comparison with corresponding homozygous rats. The data obtained thus provide direct evidence that the presence of endogenous VP plays no role in the concentrating ability of suckling rats as suggested from earlier indirect observations¹⁻⁶.

Use of Indomethacin to Reverse Neonatal Hypotension¹

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Summary. Treatment with indomethacin elevated systemic arterial pressure and pulmonary vascular resistance in hypotensive newborn goats. Indomethacin may be of value in restoration of systemic arterial pressure in stress-induced hypotension.

Systemic hypotension in the newborn may be the result of many factors including hypoxia³, asphyxia⁴, respiratory distress⁴, hyaline membrane disease^{4,5} and hemorrhage⁶. Hypotension, in part, may be the result of prostaglandin release. These experiments were undertaken to evaluate effects of indomethacin, a prostaglandin synthetase inhibitor⁷, on the systemic circulation of hypotensive newborn goats.

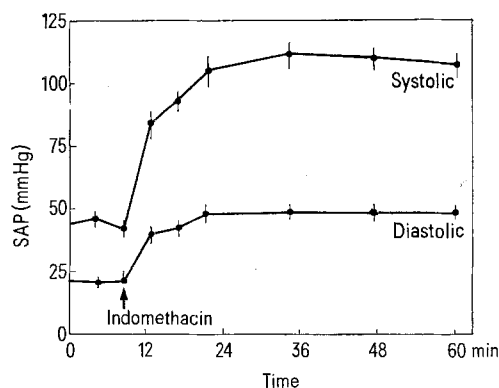
Hypotension (mean pressure less than 32 mm Hg in the descending aorta) was produced in eleven newborn goats (1-7 days of age, wt. 3.0 ± 0.2 kg⁸) by periods of hypoxia, asphyxia, acidemia, prolonged anesthesia and surgery, or fluid loss. Arterial pH, P_{O_2} and P_{CO_2} were corrected (pH 7.39 ± 0.01 , $P_{CO_2} = 35 \pm 1$ mm Hg and $P_{O_2} = 160 \pm 9$ mm Hg) prior to indomethacin administration. Pulmonary vascular resistance was evaluated in 5 newborns by pump perfusing the left lung with blood from the inferior vena cava and measuring pulmonary arterial and left atrial pressures.

Treatment of hypotensive animals with indomethacin (2.4 mg/kg i.a.) increased⁹ systolic, diastolic, and pulse

pressures (Figure). Mean systemic arterial pressure increased 158% (26 ± 3 to 67 ± 5 mm Hg). Heart rate and pulmonary vascular resistance increased 8% (165 ± 9 to 178 ± 10) and 37% (0.79 ± 0.14 to 1.08 ± 0.19 mm Hg · kg · min/ml), respectively. These effects of indomethacin on cardiovascular dynamics persisted for the duration of monitoring (3 h).

Indomethacin was effective in reversing systemic hypotension in all animals studied. This vasopressor response may be a consequence of the removal of a direct vaso-depressor action of prostaglandins on systemic vasculature or removal of inhibition due to prostaglandins of sympathetic vasoconstrictor activity¹⁰. [In preliminary experiments, treatment with indomethacin increased mean systemic arterial pressure only 12% following phentolamine administration (4 mg/kg, $n = 3$).]

These results suggest that indomethacin may be useful in reversing stress induced hypotension. Thorough consideration of effects of indomethacin on pulmonary vascular resistance is indicated before indomethacin is used in the newborn.



Effect of treatment with indomethacin (2.4 mg/kg i.a.) on systemic arterial pressure (SAP) of 11 newborn goats with stress-induced hypotension. Results are means \pm SE.

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⁸ Mean \pm SE.

⁹ All differences cited are significant at $p < 0.05$ (*t*-test).

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