It may be argued, however, that a change of the cable properties could give similar results to those described above. In order to test this possibility the electrical properties of RN cell membranes were assessed by analysing the membrane transients induced by current pulses through the microelectrode. No significant changes were found between normal cats and those with chronic IP lesion. The possibility of attributing the change of the time course of CP-EPSPs following IP destruction to any change of the electric membrane properties thus seems refuted. A denervation supersensitivity could possibly be responsible for an increase of amplitude of the CP-EPSPs, but fail to explain the change in their time course.

Further experiments, including a study of the time course of sprouting, must however be performed before it is possible to relate the present findings with the well-known compensation after cerebellar lesions.

Résumé. Après destruction chronique de la projection rubrale (somatique) interpositionnelle, on constate par examen électrophysiologique que le système cortico-rubral dendritique est de toute évidence capable, par bourgeonnement, de rétablir des contacts synaptiques avec la région «dénervée» des cellules RN.

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Inactivation of Prostaglandin E_1 by Lungs of the Foetal Lamb

Prostaglandins of E and F types undergo substantial inactivation during passage through the pulmonary vascular bed of the adult animal[1-7]. Most probably, the loss of activity results from degradation of the compounds by specific enzymes endogenous to lung tissue[6]. We report here that lungs of foetal lambs possess similar inactivating properties.

Material and methods. Suffolk foetal lambs of known gestational age (111 to 142 days; term is 147 days) were exteriorized with the mother under methoxyflurane-nitrous oxide anaesthesia. Placental circulation was preserved while spontaneous ventilation was prevented by covering the head with a saline-filled rubber glove. Newborn (11–12 days from birth) and 6-month-old lambs were anaesthetized with sodium pentobarbital (30 mg/kg given i.v.), and anaesthesia was maintained with a mixture of methoxyflurane-nitrous oxide-air under positive pressure ventilation.

The great vessels were exposed through a left thoracotomy and the ductus arteriosus of foetal and newborn lambs was ligated. A polyethylene tube was inserted into the main pulmonary artery (foetal and newborn lambs) or in the right atrium of older animals (*pre-pulmonary catheter*). A second catheter was introduced retrogradely into the left common carotid artery and positioned in the ascending aorta just above the aortic valve (*post-pulmonary catheter*). Systemic blood pressure was recorded from the thoracic aorta using a catheter advanced from a femoral artery. A Statham strain gauge (P 23 Db) coupled to a Brush chart recorder model 200 served for this purpose. Blood gases and pH were measured with an Instrumentation Laboratory analyzer model 113 in samples from the thoracic aorta.

Prostaglandin E_1 (PGE_1) solutions were made up in saline by dilution of a 10 mg/ml ethanol-water (95:5 by vol.) stock solution. Concentrations varied between 4 and 64 µg/ml depending on the weight of the animal. PGE_1 was infused alternately into the pre- and post-pulmonary catheters at a variable rate (0.02–3.88 ml/min) with a Harward pump model 940. Each infusion lasted 2 min and 15 to 30 min intervals were allowed between administrations. In each experiment, the response to the first infusion was excluded from the final results to minimize possible errors due to tachyphylaxis.

Results and conclusion. Occlusion of the ductus arteriosus in foetal lambs produced a partially reversible fall in systemic blood pressure. After stabilization, the systolic blood pressure ranged from about 50 mm Hg at 111 gestation days to 70–100 mm Hg near term. The blood pressure was between 102 and 125 mm Hg in the newborn and 6-month-old lamb. In all animals, PGE_1 had hypo-

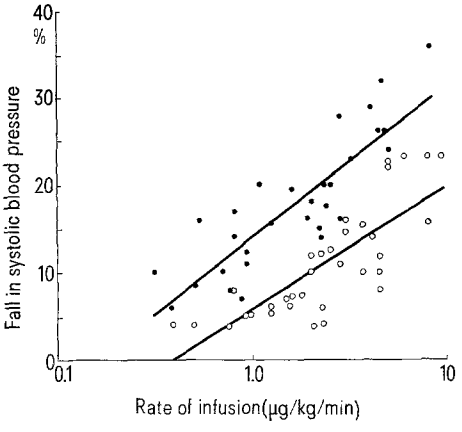
Pulmonary inactivation of prostaglandin E_1

Animal	Weight (kg)	Loss of activity (%)	Mean loss (± S.E.)
Foetal lamb	2.2	62	—
111, 113 gestation days	2.5	52	
Foetal lamb	3.1	76	
126–142 gestation days	3.9	56	
	3.3	64	72 ± 5[a]
	3.4	62	
	4.2	86	
	4.9	89	
Newborn lamb	4.6	87	
11, 12 days	5.1	97	84 ± 6[a]
Six-month-old	17	69	
lamb	33	85	

In each experiment, sequential dose-response curves were obtained with PGE_1 infused into the aorta and pulmonary artery (or right atrium). The percentage inactivation is given by [100-($D_a/D_{pa} \times 100$)] where D_{pa} and D_a are the doses of PGE_1 required to produce an equal fall in systemic blood pressure by the pre- and post-pulmonary routes, respectively. Rates of infusion into the pre- pulmonary line were 0.38–9.50 µg/kg/min (foetal lambs) and 0.37–7.60 µg/kg/min (newborn and 6-month-old lambs). PO_2 of thoracic aorta blood was 15–26 mm Hg (mean 21) in foetuses and 92–160 mm Hg in animals after birth. Values of pH below 7.25 were corrected with a slow i.v. infusion of a 7.5% sodium bicarbonate solution. [a] Difference between means is not significant using Student's *t*-test.

[1] E. W. HORTON, I. H. M. MAIN and C. J. THOMPSON, J. Physiol., Lond. *180*, 514 (1965).
[2] L. A. CARLSON and L. ORÖ, Acta physiol. scand. *67*, 89 (1966).
[3] S. H. FERREIRA and J. R. VANE, Nature, Lond. *216*, 868 (1967).
[4] J. C. MCGIFF, N. A. TERRAGNO, J. C. STRAND, J. B. LEE, A. J. LONIGRO and K. K. F. NG, Nature, Lond. *223*, 744 (1969).
[5] E. W. HORTON and R. L. JONES, Br. J. Pharmac. *37*, 705 (1969).
[6] P. J. PIPER, J. R. VANE and J. H. WYLLIE, Nature, Lond. *225*, 600 (1970).
[7] N. PAPANICOLAOU and P. MEYER, Rev. Can. Biol. *31*, 313 (1972).

tensive action and the response was dose-related. As indicated by the Table, the fall in systolic blood pressure was most marked with intra-aortic infusions. The mean inactivation of PGE_1 upon passage through the pulmonary vascular bed was 72% in foetuses of gestational age from 126 days onwards. This value does not differ significantly from that obtained in newborn and 6-month-old lambs. Two successful experiments were performed in foetuses at an earlier stage of gestation (111 and 113 days), that is prior to the appearance of surface-active material in lung tissue[8]. In these animals, the lungs were still capable of PGE_1 inactivation. However, the percent loss of PGE_1 activity (52 and 62%) was in the low range of values obtained with older foetuses, suggesting a less efficient mechanism of inactivation. More results are needed to clarify this point.



Dose-response lines for PGE_1 infused into the aorta (●) and the pulmonary artery (○) of foetal lambs (111–142 gestation days). Each point applies to a single response. Calculated regression equations are $y = 18.06 \log x + 13.89$ (●) and $y = 14.05 \log x + 5.94$ (○).

The Figure illustrates the dose-dependent relation for PGE_1 given by pre- and post-pulmonary routes to foetal lambs. Regression lines were calculated with a least squares fit on pooled data from all experiments (8 animals, see Table). The 2 slopes did not depart significantly from parallelism, whereas the difference between the intercepts was significant ($P < 0.01$). Pulmonary inactivation calculated from the regression equations is 73%.

These experiments demonstrate that lungs of foetal lambs inactivate PGE_1 from 111 days gestation onwards and that the degree of inactivation is the same with mature foetuses and animals after birth. By inference from work with adult animals[6], we postulate that an enzymic process is responsible for the loss of PGE_1 activity. If PG-degrading enzymes develop similarly in lungs and other organs (e.g. liver), then it follows that also in foetuses near term PGE and PGF compounds are not fitted to the role of circulating hormones[9].

Résumé. Le poumon de l'agneau foetal a la propriété d'inactiver la prostaglandine E_1 à partir du 111ème jour de gestation (terme: 147 jours). Le degré d'inactivation, chez le foetus près d'être à terme, est de l'ordre de ce qu'on observe dans le poumon du nouveau-né et de l'agneau de 6 mois.

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[8] W. F. Howatt, M. E. Avery, P. W. Humphreys, I. C. S. Normand, L. Reid and L. B. Strang, Clin. Sci. *29*, 239 (1965).

[9] This work was supported by the Medical Research Council of Canada (grants No. MA-3310 and No. MA-3912). We thank Dr. J. E. Pike (Upjohn Company) for PGE_1, and Mr. F. Hamilton for technical help.

Rest-Activity Cycle and Sleep Patterns in Captive Foxes (*Vulpes vulpes*)

Comparative studies on sleep indicate that security of environment is the main factor influencing the amount of total sleep time (TST) and in particular the percentage of paradoxical sleep (PS). Allison and Van Twyver suggest that animals which rest normally underground or in a den are 'secure' sleepers, and that they will sleep readily under laboratory conditions[1]. This present work has been carried out on the fox, which apart from its predatory activity lives mainly in an earth.

Methods. Three foxes (2 ♂, 1 ♀); captured at the age of 2 months, were kept in a large cage which contained a smaller cage serving as a den. The animal were fed once a day (08.00 h) with canine food cubes and received water ad libitum. When they were 1 year old, their 24-h activity cycle was recorded on a kymographic apparatus from transducers placed under the support of the cage. The ECoG activity was next obtained from 3 pairs of silvered screws inserted under pentobarbitone anaesthesia (30 mg/kg) over the frontal, parietal and occipital cortex at 2 cm on either side of the sagittal suture. Electrodes were inserted into the neck muscles for electromyography. 2 screws fixed on the fifth rib on each side enabled recording of heart rate and by impedance changes the respiratory movements. A polygraph (Reega VIII Tr. Alvar) was used to obtain a continuous record during a week from the time after the surgical procedure. The first

[1] Tr. Allison and H. Van Twyver, Expl Neurol. *27*, 564 (1970).

Sleep pattern characteristics and cardio-respiratory rates (mean value ± SE) in the fox

	Awake	Drowsiness	Slow wave sleep	Paradoxical sleep
Mean percentage per day	38.9	20.3	30.8	10.0
Individual periods — Length (min)	—	4.9 ± 0.36	8.9 ± 0.73	5.1 ± 0.42
Individual periods — Number (per day)	—	59 ± 12	45 ± 11	28 ± 5
Heart rate (min) ($n = 10$)	101.7 ± 3.3	77.2 ± 0.6	77.7 ± 1.0	92.0 ± 1.7
Respiration rate 30 sec ($n = 10$)	12.9 ± 0.67	10.4 ± 0.40	9.9 ± 0.35	10.5 ± 0.48