newborn galagos have only thin fur on the back and a hairless belly. Their insulation is very poor. Not until the age of 3–4 weeks do bushbabies develop dense fur. Up to 20 days there was no kind of behavioral thermoregulation and the young ones depend on the thermal protection of their parents. Immediately after bring out of the nest box, the rectal temperature of the newborn bushbabies varied from 33.4 to 35.4 °C; at the 11th day it reached 36 °C, or a little more. The rectal temperature of the adults, however, averages 36.4 ± 0.5 °C during resting period. The newborn bushbaby has only a small range of temperature regulation. When removed from the nest box, body temperature drops down to 32 °C within 5 min (ambient temperature 25 °C). After a cold exposure of 30 min (15 °C ambient temperature) the newborns reacted with a decrease in body temperature of 7 °C and shivering was distinctly noticed. The metabolic rate at the 1st to 3rd day was higher than at the day of birth. The metabolic reaction to ambient temperatures from 25 to 15 °C is clearly developed: The maximum values are between 5 and 6 ml O_2/g · h; this is more than twice the basal metabolic rate measured at 30 °C. The RQ-values reached 0.7–0.8 and indicate a strong fat metabolism. During the following weeks, the metabolic reactions decrease and after 15 weeks are reduced by 50%. This is mainly caused by the reduction of heat flow in relation to body weight and by increased thermal insulation. After 140 days the metabolic rate of the twins reached the level of the adults (0.79 ml O_2/g · h, neutral temperature zone 26–35 °C) which is about 17% below the value calculated from the KLEIBER[2] formula. The difference of oxygen consumption between ambient temperatures of 25 and 20 °C is strongly reduced from the 4th week. Both indicate an expansion of the neutral temperature zone in the direction of lower ambient temperatures. Considering only the minimal metabolic values (30 °C ambient temperature) a steady decrease from the 5th day (2.9 ml O_2/g · h) to the 140th day (0.7 ml O_2/g · h) is noticed. Compared with the KLEIBER[2] curve, the minimal metabolic values lie above the curve from the 5th day to the 9th week; they reach and remain under the curve between the 10th and 11th week till the level of the adults is established.

Inspite of the intense increase of heat production in the first days of life, the large newborns (body weight of newborns: adult weight = 1:12) are unable to compensate the heat loss at ambient temperatures between 25–15 °C; as a consequence body temperature decreases. The unfavorable relation of surface/volume and the low thermal insulation necessitate 4 weeks to stabilize body temperature. The intensive heat production of the young ones, which agrees with the maximum metabolism of the adults in percent, leads to the conclusion that the temperature-regulating system already operates completely but with insufficient capacity and that it is developed in a similar way to that of human newborn infants[3–6].

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Meclofenamate Does not Reduce Chronic Hypoxic Pulmonary Vasoconstriction

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Summary. There was no reduction in the pulmonary pressor response to hypoxia following inhibition of prostaglandin synthesis in rats exposed to chronic hypoxia. A fall in left ventricular weight suggested that systemic pressure may have been reduced after inhibition of prostaglandin synthesis in normoxic rats.

Alveolar hypoxia induces pulmonary vasoconstriction. It is not known whether the reaction is a direct effect of hypoxia on the vascular smooth muscle or if it requires a chemical mediator. Possible mediators include histamine, norepinephrine, and 5-hydroxytryptamine. It has been proposed recently by LILJESTRAND[2], PIPER and VANE[3], and SAID et al.[4] that protaglandins (PG) also be considered. We have shown that PG's do not mediate the pulmonary pressor response to hypoxia in acute studies with the awake calf, anesthetized dog, and the isolated perfused rat lung, and they may even offer protection against it. This study examined the role PG's in the pulmonary vascular response to chronic hypoxia.

Method. In the experiment, 25 female Sprague Dawley rats weighing 70 to 100 g were used. They were divided into 4 groups: 1. 4 rats, normoxic and untreated (NN); 2. 4 rats, normoxic and treated with meclofenamate (NM); 3. 8 rats, chronically hypoxic and untreated (HN); 4. 9 rats, chronically hypoxic and treated with meclofenamate (HM).

Groups NM and HM were injected with 10 mg/kg meclofenamate i.p. twice a day in order to inhibit PG synthesis. This dose is in excess of that required to maintain a plasma level of meclofenamate sufficient to inhibit PG formation. Indomethacin is approximately 20 times as potent as aspirin in inhibiting PG synthesis in lung tissue[5]. Meclofenamate is considered more potent that indomethacin[6].

[1] This work was supported by NIH grant No. HL 14985.
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At the beginning of the experiment, groups HM and HN were placed in a hypobaric chamber and brought to a simulated altitude of 3660 m (485 mm Hg) and after 2 days, to 4600 m (428 mm Hg). 2 days later, they were raised to 5500 m (380 mm Hg) where they remained for the rest of the study. They were returned to Denver pressure (635 mm Hg at 1600 m) for about 20 min twice each day to permit cleaning of the cages and administration of meclofenamate injections. The temperature of the chamber was kept about 27 °C and frequent checks found the level of CO_2 to be 0.01% or less. All the rats had free access to food and water, and fresh air was constantly circulating through the hypobaric chamber.

After 5 weeks under these conditions, each rat was anesthetized with i.p. sodium pentobarbital, the trachea cannulated, and the lungs fixed in situ with 3.4% gluteraldehyde from a height of 20 cm. The lungs and heart were removed and sections of the lung were taken for histological examination. The medial thickness of the small arteries (30–450 μm diameter) in the lungs was measured. The atria were carefully removed from the ventricles which were then separated from each other, the septum (S) remaining with the left ventricle (LV). The right ventricle (RV) was weighed separately from the LV and S. The ratio LV + S/RV was then calculated. A decrease in this ratio indicates right ventricular hypertrophy, presumably secondary to increased pulmonary arterial pressure.

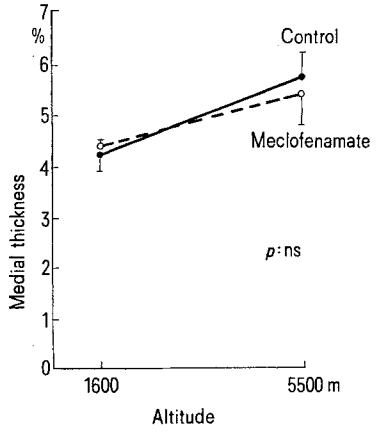

Fig. 1. Meclofenamate does not alter the medial thickness response to chronic hypoxia.

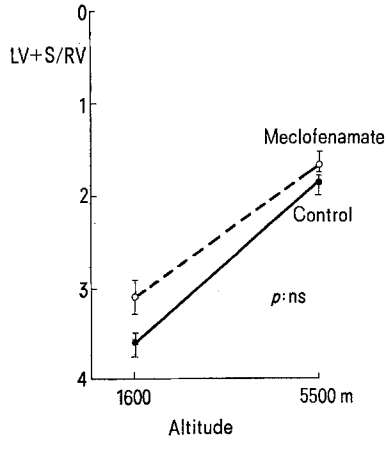

Fig. 2. Meclofenamate does not alter the right ventricular hypertrophy response to chronic hypoxia.

Statistics. The mean and standard error of the mean are given for all data. Comparisons between groups are made by the two-tailed unpaired *t*-test and comparisons within groups by the paired *t*-test. Differences were considered significant when $p < 0.05$.

Results. The chronically hypoxic rats showed a significant increase in medial thickness and right ventricular hypertrophy (as measured by the ratio LV + S/RV) when compared to the normoxic rats. However, as shown in Figures 1 and 2, there was no difference between the treated and untreated rats.

The rats at high altitude showed a smaller increase in weight (mean increase +113 g) than those outside the chamber (+143 g). The treated rats at low altitude had significantly lower left ventricular weights (363 ± 7 mg) than the untreated group (435 ± 42 mg). When corrected for the variation in body weight (LV + S/BW), this difference was still significant (Treated 1.88 ± 0.05 vs. Untreated 2.23 ± 0.08). There was no difference between the two groups at high altitude.

Discussion. HEATH et al.[7] and ABRAHAM et al.[8] examined the effect of the same altitude and duration of hypoxia on Wistar rats. The ratio LV + S/RV which they recorded (normoxic 4.5 and 4.3 and hypoxic 1.8 and 1.7), were similar to the combined normoxic, 3.4, and hypoxic, 1.8, measurements for treated and untreated groups in our study. The increase in % medial thickness which we observed (normoxic 4.3 and hypoxic 5.5) was similar to that of HEATH et al.[7] (3.4 and 4.3) but less than that reported by ABRAHAM et al.[8] (5.0 and 9.0).

SAID et al.[4] found that aspirin reduced the pulmonary pressor response to hypoxia in the isolated perfused cat lung and that a PG-like substance was present in the venous effluent during hypoxia. He concluded that PG's might help to mediate the pressor response to hypoxia. In subsequent experiments using indomethacin, he found that the increase in PVR during hypoxia was not reduced[9]. In similar acute experiments in the anesthetized dog, we have demonstrated that following inhibition of PG synthesis with meclofenamate or indomethacin, the pressor response is actually augmented[10].

In the present experiments, in rats treated over 5 weeks with meclofenamate, there was no evidence of a fall in the hypoxic pulmonary vasoconstriction as reflected by changes in right ventricular weight and pulmonary arteriolar medial thickness. Thus, it is unlikely that PG's mediate the acute or chronic response of the pulmonary vasculature to hypoxia.

In the normoxic rats in which PG synthesis was prevented, left ventricular weight was reduced. In rabbits treated with indomethacin (10–20 mg/kg/day) for 17 days, systemic arterial pressure was found to be elevated compared to untreated controls (McGIFF[11]). One explanation for this is that in rabbits endogenous PGE_2 dilates the renal arteries. Inhibition of PG synthesis might then lead to renal vasoconstriction and secondary systemic hypertension. In the rat, however, PGE_2 constricts the renal arteries and removal of this effect might be expected to result in renal vasodilatation and a fall in systemic arterial pressure. It may be that the reduction in LV weight, that we observed, reflects such a fall in pressure.

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