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Influence of Altitude and Age on Pulmonary Arterial Pressure in Cattle (39079)

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Animals and humans living permanently at high altitudes must adapt to chronic hypoxia. The extent to which this is attained appears to depend not only upon the level of altitude and hypoxia but also the species involved and the genetic–evolutionary makeup of its members.

It has been known for many years that less than 2% of the native cattle living at the higher mountainous elevations in Colorado develop right heart failure, e.g., high mountain or brisket disease, while at the same altitudes up to 40% or more of the cattle native to low altitudes contract the disease (1). Although cattle of all ages are affected the greatest incidence of high mountain disease is in calves less than 1 yr old. Collectively, this evidence has suggested that at high altitude, native animals probably have lower levels of pulmonary arterial pressure than cattle introduced from low altitudes and furthermore, young animals probably have higher pressures than adult animals. There have been no reports, however, of a systematic study of pulmonary arterial pressure in healthy cattle native to high altitude.

The purpose of this study was to determine by actual measurements whether cattle native to different altitudes have different levels of pulmonary arterial pressure and whether age is an influencing factor.

Materials and methods. Pulmonary arterial pressures were determined by direct cardiac catheterization on a total of 195 cattle under two classifications, age and altitude. Animals of three age groups; 3 months–1 yr, 1–3 yr, and 3–10 yr were studied at four altitudes: sea level (New Bolton Center, Pa.), 1524 m (Fort Collins, Colo.), 2590 m (near Saratoga, Wyo.), and 3048 m (near Fairplay, Colo.).

Animals studied at the two higher altitudes were females of the Hereford breed selected from permanent ranch herds. Those studied at 1524 m were Herefords native to this or slightly lower altitudes with the oldest age group made up of females and the two younger groups of both sexes. At sea level the animals were females of the Jersey breed. Most ages within the ranges of the three age groups were represented by one or more animals except at sea level where the three animals in the upper age group were close to 10 yr of age.

The catheterization procedure was performed as previously described (2) with the animals unmedicated and held in a normal standing position in a standard cattle chute or, at sea level, in a stanchion. With the animal's head held to one side with a rope halter, a PE 190 polyethylene catheter was passed percutaneously, under local anesthesia, through an 11-gauge needle via the external jugular vein and right heart to the main pulmonary artery. Catheter position was determined by the form of the pressure waves. Pulmonary arterial blood pressure was recorded using a standard strain-gauge pressure transducer and direct writing oscillograph. Zero reference point for the transducer was at the level of the olecranon with the animal in normal standing position (3).

Although the restraint and catheterization procedures usually produced brief excitement and a transient rise in pulmonary arterial pressure, sufficient time was allowed for the pressure to stabilize before measurements were made. The average of two or more similar pressures, recorded several minutes apart was tabulated for each animal. Mean pulmonary arterial pressure was determined by planimetry.

Statistical analysis of the data on mean pulmonary arterial pressures consisted of a two-way analysis of variance (ANOVA) with

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TABLE I. MEAN PULMONARY ARTERIAL PRESSURE OF THREE AGE GROUPS OF CATTLE AT FOUR ALTITUDES.

Age	Sea level	1524 m	2590 m	3048 m
3 mo–1 yr	28.0 ± 2.6[a] (n = 3)	30.1 ± 0.7 (n = 10)	28.5 ± 1.2 (n = 15)	34.8 ± 1.4 (n = 66)
1–3 yr	30.2 ± 2.5 (n = 6)	27.4 ± 1.4 (n = 10)	28.9 ± 1.2 (n = 16)	41.4 ± 1.8 (n = 30)
3–10 yr	34.3 ± 1.9 (n = 3)	29.8 ± 1.3 (n = 4)	38.2 ± 1.7 (n = 15)	37.5 ± 1.9 (n = 17)

[a] Group means ± SE (mm Hg).

TABLE II. FINAL ANALYSIS OF VARIANCE BASED ON WEIGHTED SQUARE OF MEAN TECHNIQUE.

Source	df	SS	MS	F ratio
Total	194	17900.585		
Error	183	14061.666	76.840	
Treatments	11	3838.919	348.993	4.542[a]
Altitude	3	2000.384	666.795	8.678[a]
Age	2	278.392	139.196	1.812[b]
Age × Altitude	6	1560.143	260.024	3.384[a]

[a] Significant at $P < 0.001$.
[b] Not significant.

unequal numbers and two classifications, age and altitude. A preliminary ANOVA was made of significance for interaction between age and altitude on pulmonary arterial pressure with a follow-up analysis of their separate effects on pressure by the weighted square of means technique (4).

Results. Examination of data on mean pulmonary arterial pressure for the three age groups at four altitudes (Table I) revealed a tendency for the pressure to be increased with both increasing age and altitude. The preliminary ANOVA showed a significant F ratio ($P < 0.001$), indicating an interaction effect of age and altitude on pulmonary arterial pressure.

The weighted square of mean analysis for the separate effects of age and altitude (Table II) showed that altitude had a significant effect on the pressure. The overall effect, as seen in Table I, was an increase in pressure with increasing altitude with significance only above 2590 m.

Age was not shown to have a separate effect on pressure (Table II). However, on considering the interaction between age and altitude (Table I), it was found that at the altitude of 3048 m the two groups of older animals, ages 1–3 yr and 3–10 yr, had higher pressures than did the younger animals. Also at 2590 m altitude the 3–10-yr-old animals had higher pressures than did the two younger groups. Age appeared to have no clear effect at 1524 m and at sea level. A comparison of the data averaged for the two lower and two higher altitudes, respectively (Fig. 1), indicates that pulmonary arterial pressure probably increased with age at the higher but not lower altitudes.

Discussion. Previous studies demonstrated that when cattle native to low altitudes are taken to altitudes approximating 3000 m, they develop moderate to severe pulmonary hypertension (Fig. 2), often accompanied by right heart failure, a syndrome commonly known as high mountain or brisket disease (3, 5). Further, over the last ten years, two groups of cattle have been selectively bred to show traits either of "susceptibility" or of "resistance" to hypoxic pulmonary hypertension and heart failure (2, 6). Thus these traits have been shown to be transmitted from parents to offspring. One of the principal findings of this study was the remarkably low levels of pulmonary hypertension in native cattle living at altitudes up to 3048 m.

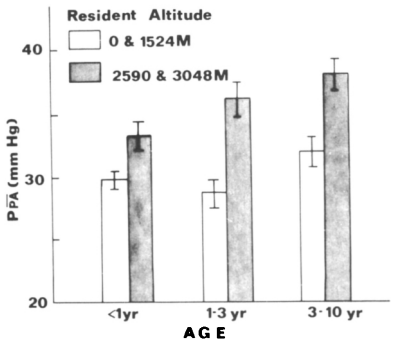

FIG. 1. Mean pulmonary arterial pressure ± SE in cattle of three age groups averaged for two low and two high altitudes.

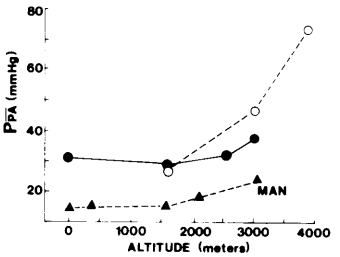

FIG. 2. Augmented pulmonary hypertension in cattle that were newcomers to high altitude. Pulmonary arterial pressure in yearling steers (3, 5) native to 1000 m after 2 months residence at 1524, 3050 and 3920 m (open circles). Values for native cattle at altitudes near sea level, 1524, 2590 and 3048 m (closed circles). Pressures measured in man (7) residing at different altitudes, are indicated (closed diamonds).

The large difference in pulmonary artery pressure between cattle which are native and those which are newcomers to high altitude is shown in Fig. 2. It seems clear that cattle native to high altitudes are more resistant to hypoxic pulmonary hypertension than those native to low altitudes.

The resistant and susceptible traits are probably genetically determined. Cattle which are born at high altitude and are susceptible to pulmonary hypertension usually develop symptoms within a few months. Thus the incidence of brisket or high mountain disease in native high altitude cattle is usually greatest in animals less than one year of age (1). Such animals would either die, or be transported to lower altitudes, before producing offspring. As a result of this selective process, the cattle population remaining at high altitude would after several generations have lower pulmonary arterial pressures as was documented in the present study. The lower pressures would in turn account for the reduced incidence of brisket disease in herds native to high altitude. It is as though pulmonary hypertension at high altitude is a maladaptation which is removed by the processes of selection.

Man is the only other mammalian species in which measurements of pulmonary arterial pressure have been made in native residents at different altitudes. The available data in humans native to high altitude in the United States (7) compared with the present data in native high altitude cattle (Fig. 2) indicate that pulmonary arterial pressures are lower in man than in cattle, but are similarly related to altitude in both species.

The evaluation of pulmonary arterial pressure as related to age in the present study was probably not affected by the well-known early pulmonary hypertension in the neonate. In "resistant" calves living at 1524 m altitude, pulmonary arterial pressures were shown to fall to stable values by 10 days following birth (2). All calves in the present study were 3 months of age or older.

Although a separate effect of age on pulmonary arterial pressure was not found, the data showed an interaction effect between age and altitude on pulmonary arterial pressure. It appeared that pulmonary arterial pressure increased with increasing age at high altitude, but not at low altitude. This implies that in the absence of a hypoxic stimulus, as at low altitude, age has little or no effect on pulmonary arterial pressure. A further implication is that the chronic hypoxia of high altitude acts to increase pulmonary arterial pressure in all cattle, but in newcomers the rate of increase can be measured in weeks and months, whereas in native cattle it requires several years. Thus the difference between the native high altitude cattle and the newcomers to high altitude may reside both in the magnitude of the pulmonary pressor response to hypoxia and in its rate of progression.

Summary. Pulmonary arterial pressures in native cattle ranging in age from 3 months to 10 yr were found to be increased with in-

creasing altitudes of residence from sea level to 3048 m. At altitudes of 2590 and 3048 m, but not at sea level or 1524 m, the pressures were higher in older than in younger cattle. The magnitude of the pulmonary arterial pressure, and probably the rate of progression of pulmonary hypertension at high altitude, were much less in native cattle than in cattle that were newcomers from low altitude. Natural and artificial selection are believed to have minimized the level of pulmonary hypertension in native high altitude cattle, thus protecting them from high mountain or brisket disease.

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