output may be better sustained in birds during exercise in hypoxia. Birds do not have a higher hemoglobin-O₂ affinity in general, but the affinities of several highland species are enhanced compared with lowland birds (18), which should further improve O₂ delivery during hypoxia. The flight muscle of birds also has a superior capacity for O₂ diffusion than the locomotory muscle of mammals, largely due to a high degree of branching between adjacent capillaries (14), and this capacity is increased even further in the highest flying species (19). These differences should increase the overall ability to supply O₂ to the active muscle during exercise in hypoxia.

Conclusions

Better able to tolerate and exercise in hypoxia, we conclude that birds are far superior to mammals at adapting and thriving at high altitudes. This should not be surprising when considering that the ability to fly has for millions of years enabled birds access to altitudes that were unattainable to humans and other mammals. Perhaps the simplest explanation for why birds excel at elevation is that evolution has had much more time and reason to equip them with the physiology to do so!

REFERENCES


Graham R. Scott
Jessica U. Meir
Lucy A. Hawkes
Peter B. Frappell
William K. Milsom
1Department of Biology
McMaster University
Hamilton, Ontario, Canada
e-mail: scottg2@mcmaster.ca
2School of Biology
Scottish Oceans Institute
University of St Andrews
East Sands, St Andrews, UK
3Department of Zoology
University of British Columbia
Vancouver, British Columbia, Canada
4School of Biological Sciences
Bangor University
Bangor, Gwynedd, UK
5School of Zoology
University of Tasmania
Hobart, Tasmania, Australia

COUNTERPOINT: HIGH ALTITUDE IS NOT FOR THE BIRDS!

The best evidence for the adaptation of a species to its environment is that it reproduces efficiently and passes genes to future generations. This has occurred in mammals and birds resident at...
high altitude, despite the low oxygen availability, which is challenging at all stages of life.

High altitude-adapted bird embryos have different strategies to withstand the low \( O_2 \) milieu imposed by hypobaria (3, 9, 22, 28, 30). Independent of the strategy used to achieve \( O_2 \) homeostasis, the bird embryo demonstrates some fragility at high altitude, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude develop at comparatively relative ease in this extreme environment. A well-studied example of successful mammalian evolution in the Andean altiplano is the llama.

The fetal llama. The llama fetus has not only to withstand the low arterial \( PO_2 \) of fetuses of all species relative to the maternal solution in the Andean altiplano is the llama. Developing at comparatively relative ease in this extreme environment, in which the embryo and fetus adapted to high altitude, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude develop at comparatively relative ease in this extreme environment. A well-studied example of successful mammalian evolution in the Andean altiplano is the llama.

The oxygen and nutrient exchange is improved in the camelidae, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude develop at comparatively relative ease in this extreme environment. A well-studied example of successful mammalian evolution in the Andean altiplano is the llama.

The oxygen and nutrient exchange is improved in the camelidae, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude develop at comparatively relative ease in this extreme environment. A well-studied example of successful mammalian evolution in the Andean altiplano is the llama.

The oxygen and nutrient exchange is improved in the camelidae, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude, which contrasts markedly with the more-resilient duo that represent the mammalian mother and placenta combination, in which the embryo and fetus adapted to high altitude develop at comparatively relative ease in this extreme environment. A well-studied example of successful mammalian evolution in the Andean altiplano is the llama.

The neonatal llama. Pulmonary hypertension can be a major problem for neonates born at high altitude. This is due to the dramatic pulmonary vasodilation that needs to take place at birth in a low oxygen environment, as hypoxia tends to produce pulmonary vasoconstriction. The fetal llama is somewhat protected from pulmonary hypertension by having a higher sensitivity to a vasodilator (NO) and a lower sensitivity to a vasoconstrictor (NE) than the fetal sheep, consistent with a lower pulmonary arterial pressure measured in the neonatal llama compared with lowland species, e.g., sheep. E, epinephrine; NE, norepinephrine; AVP, arginine-vasopressin; NPY, neuropeptide Y; ETA, endothelin A receptor; NO, nitric oxide; CO, carbon monoxide; HO-1, heme oxygenase-1; PHT, pulmonary hypertension; PAP, pulmonary arterial pressure; SMC, smooth muscle cells; ↑, increased; ↓, decreased.

Fig. 1. Cardiovascular and metabolic adaptations of the llama at different stages of development compared with lowland species, e.g., sheep, E, epinephrine; NE, norepinephrine; AVP, arginine-vasopressin; NPY, neuropeptide Y; ETA, endothelin A receptor; NO, nitric oxide; CO, carbon monoxide; HO-1, heme oxygenase-1; PHT, pulmonary hypertension; PAP, pulmonary arterial pressure; SMC, smooth muscle cells; ↑, increased; ↓, decreased.
with the newborn lamb in the Andean altiplano (20). Moreover, newborn llamas showed a marked increase in pulmonary carbon monoxide (CO) production and heme oxygenase-1 (HO-1) expression at high altitude, resulting in pulmonary vasodilatation compared with sea level llama and sheep neonates (12). This results in protecting the pulmonary vasculature of the llama against the deleterious effects of chronic hypoxia, namely hypoxic pulmonary vasoconstriction and vascular remodeling (12). The pulmonary HO-CO system action is mediated by cGMP and BKCa channels, resulting in an effective mechanism in the regulation of this vascular bed (12).

We could not find comparable information in hatchlings of high-altitude birds.

**Adult llamas.** Among the physiological adaptations of the adult llama that allow it to live under conditions of oxygen limitation at altitude are: low P50 (21), small elliptical red cells with high hemoglobin concentration (14), slight increase in blood hemoglobin concentration (1), high muscle myoglobin concentration (26), a more efficient O2 extraction at tissue levels (1), and high lactic dehydrogenase activity (26). Furthermore, the adult llama avoids pulmonary arterial hypertension and cardiac remodeling (24), among other adverse effects, by having less muscularized pulmonary arteries than the adult sheep (10). These alterations comprise a cassette of beneficial adaptations in the Andean llamas to the chronic hypoxia of life at high altitude (Fig. 1) (19).

Preventing high-altitude pulmonary hypertension is a central feature to be accomplished, permanently by the ground-based llamas and temporarily by the high-flying bar-headed geese, both facing the low O2 milieu found in very high altitudes (5).

**Conclusions.** Combined, the available data at the physiological, cellular, and molecular levels strongly demonstrate a variety of successful evolutionary adaptive strategies in the llama, as a high-altitude-adapted mammal, which thus far have not been replicated in embryos and in hatchlings of high-altitude birds.

**REFERENCES**


Avian embryos and have been well reviewed (2). For example, various steps of the oxygen transport cascade in high-altitude environments. Acclimatization and true adaptation occur at strategies have been described for bird embryos in hypoxic identical to those described for mammals, a suite of adaptive Andean altiplano (10). Although avian adaptations may not of the range and even well above the llama’s home in the fully between altitudes of 4,000 and 6,500 m (1, 2, 4), at the top birds, we offer support for avian supremacy in these early life stages (3). In upholding that high altitude is indeed for the point focuses on adaptive strategies at embryonic and neonatal hypoxia and exercise at high altitude (5), while the Counter- elegantly described by Llanos et al. (3), we first highlight that adaptations of the llama compared with other mammals, as

REBUTTAL FROM MEIR ET AL.

Although we do not dispute the remarkable high-altitude adaptations of the llama compared with other mammals, as elegantly described by Llanos et al. (3), we first highlight that the Point focuses on the ability of adult animals to tolerate hypoxia and exercise at high altitude (5), while the Counter-point focuses on adaptive strategies at embryonic and neonatal life stages (3). In upholding that high altitude is indeed for the birds, we offer support for avian supremacy in these early stages.

Avian embryos from several highland species hatch successfully at altitudes of 4,000 and 6,500 m (1, 2, 4), at the top of the range and even well above the llama’s home in the Andean altiplano (10). Although avian adaptations may not be identical to those described for mammals, a suite of adaptive strategies have been described for bird embryos in hypoxic environments. Acclimatization and true adaptation occur at various steps of the oxygen transport cascade in high-altitude avian embryos and have been well reviewed (2). For example, although the partial pressure of O2 in embryonic tissue may be as low as 10 mmHg in the mountain coot, growth and development at high altitude is equivalent to that at sea level in this avian species (2). Normal development at elevation probably involves modifications to both oxygen supply and demand processes in bird embryos, as shown in barred geese, whose impressive adult adaptations to high altitudes were documented in our original piece (5–7). In fact, contrary to Llanos et al.’s discussion on the “fragility” of avian embryos and contrasting resiliency of mammalian reproduction, high-altitude camelids like the llama and alpaca have an extremely variable rate of reproductive success, with ova, embryonic, and fetal mortality up to 80% (8, 9).

Most importantly, it is the greater capacity of birds to tolerate hypoxia and exercise at high altitudes that supports our assertion of avian supremacy, as described in our original manuscript (5). Despite the lack of “similar data” for bird species cited by Llanos et al., the wide range of adaptations exhibited by both avian embryos and adults clearly demonstrates their success at both beginning life and inhabiting high-altitude environments. Given these arguments, we maintain that high altitude IS for the birds!

REFERENCES


REBUTTAL FROM LLANOS ET AL.

The argument of Scott et al. (8) supporting avian superiority in tolerating hypoxia is based largely on the high flying performance of one species, the bar-headed goose, supplemented by comparisons between birds and several lowland mammals (7). A more appropriate exercise would be direct comparison between high altitude-adapted birds and high altitude-adapted mammals.

Their argument for the superiority of the bird brain in better tolerating hypoxia is based primarily on theoretical grounds, especially by the influence of low O2 and high CO2 on cerebral blood flow. We have shown experimentally that even in the lowland-derived sheep, the fetal brain has a remarkable capacity to maintain its O2 consumption by increasing its blood flow up to quite a severe degree of hypoxia, at least until a point of decompensation is reached (2). The high-altitude llama fetus uses a different strategy of cerebral hypometabolism, without apparent brain damage during hypoxia (1). This empirical evidence trumps any theoretical discussion of avian over mammalian superiority at tolerating hypoxia.

Similarly, the authors’ argument for bird superiority in pulmonary physiology is based largely on the hazards of