Case Studies in Physiology: The Case of the Giant Giraffe

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This issue of the journal marks the first Case Study article we have published (15). These articles are the physiological equivalent of clinical case reports, showcasing unusual or extreme physiology in single experimental subjects. Our vision is simple—we wish to encourage studies of rarely available subjects, not because they are rare, but when they have the potential for clarifying important concepts thanks to some unusual structural or functional feature they uniquely possess. Thus a key component of a Case Study article must be to clarify an important, general physiological mechanism; a simple description of unusual physiology will not suffice. A risk in such reports is of course presenting data from just a single subject, such that the outcome is not robust because the subject is not representative of the population. That challenge must be reasonably met by the authors by comparing signal to noise in their analysis and by the reader in recognizing the limitations of the data.

A case study might evaluate an individual world champion athlete, an astronaut who has been at the International Space Station for a year, a climber able to ascend Everest without supplemental oxygen, a wild animal whose physiology is unique and rarely accessible. This case study evaluates the gas exchange properties of a giraffe. Yes, the giraffe is rarely available for study, but that alone does not justify publication. Here, the large lungs lend themselves to exploration of the effects of gravity on ventilation and blood flow distribution; the long neck raises the question of a likely large conducting airway dead space volume and how that may alter ventilation. In this case, there is also the opportunity to evaluate the effect of anesthesia on pulmonary gas exchange compared with other species, given the large lung size.

Nyman et al. (15) used the multiple inert gas elimination technique (MIGET) to evaluate pulmonary gas exchange in a young giraffe. This opportunity arose because the animal underwent anesthesia for veterinary care. The study is notable, in part, because conducting MIGET in the presence of inhalational anesthesia is technically demanding: MIGET gases are present in parts per million, whereas the concentrations of volatile anesthetics required for anesthesia are orders of magnitude higher, interfering with the measurement of MIGET gases with chromatography. However, with care these constraints can be overcome.

Perhaps one of the most interesting applications of MIGET is in evaluating the comparative physiology of gas exchange, allowing the ability to study the relationship between lung structure and function. Across species, lung structure varies markedly—from the simple unicameral saclike structures for some reptiles to the bird lung where ventilation and gas exchange are served by different structures (16) to the alveolar lung of mammals. Remarkably, ventilation-perfusion matching is similar across species such as reptiles (7), birds (19), and mammals (18), and the difference between species is less than the differences between humans with normal lungs and patients with lung diseases (18). Nyman et al. adds to this body of literature by furthering a comparison of ventilation-perfusion matching across lungs of markedly different sized animals, from the rat (~400 g) to the giraffe, which at ~400 kg is 1,000 times larger. Based on this case report and other work, the take home message is clear—the extent of ventilation-perfusion mismatch varies little with lung size; the giraffe is not worse than a rat. Why this is the case is not apparent. Much larger gravitational effects are expected on the large lungs of the giraffe than on the small lungs of a rat. That it is not seen may be because gravity affects ventilation and perfusion similarly or because ventilation and blood flow distributions are dominated by vascular and airway structure rather than by gravity—still an area of ongoing controversy (2)!

Larger animals have larger alveoli than smaller animals (11), and in humans CT scanning studies show that lung tissue density is not constant as lung size increases (1). Rather, individuals with larger lungs have lower lung density, implying that the alveolar structures are also larger. What implications does this variation in alveolar size have for gas exchange? Comparative MIGET studies may shed light on this issue as well. Diffusion limitation of gas transport potentially occurs both at the level of the blood gas barrier and within the alveolar gas phase, where incomplete gas mixing between inspired and alveolar gas may predispose to diffusion limitation. Gas phase diffusion limitation is detected by differences in retention and excretion between cyclopropane, which has the lowest molecular weight of any gas used in MIGET and enflurane, which has the highest. This results in a systematic error and high residual sum of squares in the MIGET analysis. Gas-phase diffusion limitation is expected in situations where the diffusion distances are larger and has been reported in resting spontaneously breathing varanid lizards (7) and in anesthetized alligators (17), both of which have larger gas exchanging air spaces than mammals. Gas-phase diffusion limitation is seen in dogs that have recently undergone pneumonectomy (8) where alveolar size is larger because of compensatory hyperinflation and in horses (6), which have a large lung. Gas-phase diffusion limitation might also be expected when dead space is smaller and the homogenizing effects of dead space may be less. For all of these reasons one would predict gas-phase diffusion limitation in the giraffe but this is not seen in the present work. This case study adds another piece of information to understanding this issue but does not resolve it.

This work also allows the evaluation of the effect of anesthesia on a large lung. Humans show the rapid development of shunt and marked ventilation-perfusion mismatch under anesthesia (3, 4, 12), which arises from atelectasis (5) and is worse
in the lateral position (10). Horses, a species noted for very tight ventilation-perfusion matching in conscious adult animals, also develop marked ventilation-perfusion mismatch and, in particular, shunt with anesthesia (13). With the giraffe one might postulate that the very large lung, which is larger than that of the horse, would develop atelectasis in the dependent regions, resulting in a large shunt. Significant shunt did not develop in the giraffe and may reflect unique characteristics of the species. The lack of shunt may be because of the short duration of the anesthesia, but, arguing against this, humans typically develop shunt within 15 min of induction of anesthesia (5). Other potential reasons include lack of breathing hyperoxic gas, the semilateral recumbent posture, and the fact that the animal was spontaneously ventilating. Alternately, perhaps some structural feature of the giraffe lung is protective against the development of shunt, but this is unclear.

One final notable aspect is the low dead space in this animal. The giraffe with its very long neck is expected to have a large dead space, but this is not the case. Giraffes have a low dead space-tidal volume ratio that is explained on the basis of a relative large tidal volume combined with a narrow trachea (9, 14, 20). As this study confirms, the physiological dead space is ~700 ml, which is much lower than expected for an animal of this size. For comparison, the physiological dead space in healthy humans with an order of magnitude smaller body size is ~150 ml.

The present study is therefore much more than a simple description of giraffe gas exchange. It poses questions regarding the influence of lung size on gas exchange and, remarkably, shows that for this critical function, size may not matter. It is a nice illustration of the purpose and vision underlying Case Reports in Physiology—to go beyond mere description of physiology in unusual subjects to address basic physiological principles across species and circumstances.

DISCLOSURES

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AUTHOR CONTRIBUTIONS

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