Did differences in mitochondrial properties influence the evolution of avian and mammalian lungs?

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It is remarkable that the two great classes of vertebrates that are capable of sustained high oxygen consumptions, the birds and mammals, share many similar features of physiology but have radically different lungs. One of the most obvious differences is the mode of ventilation. In birds, the inspired air is taken into air sacs and then pumped directly through the gas-exchanging tissue, the parabronchi (4). This can be referred to as a flow-through mode of ventilation and means that some of the gas-exchanging tissue is directly exposed to the high PO$_2$ of air. By contrast, the inspired air in mammals is mixed with a large volume of resident alveolar gas, and some of this mixed gas is subsequently expired. This tidal pattern can be called a reciprocating system of ventilation, and the result is that the capillary blood is exposed to the much lower PO$_2$ of alveolar gas. Therefore, gas exchange in the bird is potentially more efficient (12).

These two ventilation systems result in other important differences of physiology. One of the most significant is that the bird has separated ventilatory and gas-exchange systems, whereas both of these functions are subserved by alveolar tissue in mammalian lungs. The mammalian pattern is flawed. For gas exchange, it is essential to have very delicate thin membranes so that oxygen and carbon dioxide can rapidly move through them by passive diffusion. By contrast, ventilation is best done by robust bellows-like air sacs such as in the bird. Using alveolar tissue for both purposes might be regarded as a shortcoming in the evolutionary process.

Another result of the two different systems of ventilation is that the terminal air spaces are very much smaller in the bird than in the mammal. The flow-through system in birds allows the smallest air spaces in the gas-exchanging tissue to be air capillaries with diameters of the order of 10–20 μm. The situation in the reciprocating systems of mammals is very different. Here the inspired tidal volume is small in relation to the resting volume of the lung, and to enable the inspired gas to reach the most distal alveoli, the terminal airways need to be relatively large to allow the transport of the inspired gas via the processes of convection and diffusion. This is the reason why the alveoli in mammalian lung are typically much larger than the air capillaries in birds. For example, in the human lung, the diameter of the alveoli is of the order of 300 μm. The result is that the gas-exchanging tissue of the bird can occupy a small space and is almost rigid, very unlike the large volume of highly distensible alveolar tissue in the mammal. One consequence of this is that the gas-exchanging tissue in the mammal is vulnerable to collapse or atelectasis, which is a serious problem under some conditions. Another consequence is that avian pulmonary capillaries are much thinner and also more uniform in thickness than in mammals (14).

These disadvantages of the mammalian compared with the avian lung raise the question of how evolution took this path. In other words, are there features of birds that gave them a selective advantage for the evolution of more efficient lungs? The hypothesis here is that the special properties of the avian mitochondria compared with those of mammals conferred a selective advantage that allowed them to develop a flow-through system resulting in a more efficient lung rather than that with the reciprocating system.

The two evolutionary paths may have begun to diverge in the Carboniferous (5), although this is not critical to the hypothesis presented here. It has been argued that mammals were derived from a group of carnivorous reptiles, the cynodonts, whereas birds descended from theraped dinosaurs (3), but the earliest evolutionary changes that resulted in the two types of lungs may have occurred long before. The Carboniferous was characterized by a much higher oxygen concentration in the atmosphere than now, perhaps as great as 35% (2). High oxygen levels are known to increase the production of reactive oxygen species (ROS), which are damaging to tissues (13). The lung is apparently particularly vulnerable. For example, Rhesus monkeys (Macaca mulatta) exposed to 100% oxygen for only 2 days develop ultrastructural changes in the pulmonary capillary endothelial cells, followed by pathological alterations in alveolar epithelial cells and the interstitium (9). Human lungs exposed to 50% oxygen for 44 h also show some changes (6).

It has recently been shown that birds and mammals differ greatly in their production and handling of ROS. Most of the ROS are generated by mitochondria (13), and avian mitochondria produce far less ROS compared with mammals. For example, when the rate of hydrogen peroxide generation was compared in mitochondrial suspensions with pyruvate/malate, the rate was nearly four times higher for rat than for pigeon mitochondria (7). Furthermore, when rotenone, which inhibits electron flow between Complex I and the ubiquinone pool, was added, there was a sharp increase in hydrogen peroxide production for both rat and pigeon heart mitochondria, but again the rates were higher in the rat than in the pigeon. The mechanism of the reduced rate of ROS production in pigeon mitochondria is apparently the low reduction state of the free radical generation site at Complex I (1).

It has also been found that some bird tissues tolerate ROS better than their mammalian counterparts. For example, cultures of renal epithelial cells exposed to 95% oxygen over the course of 6 days showed a much faster decline in cell numbers for mice compared with budgerigars (11). Consistent with this, birds are generally long lived compared with mammals of the same body mass, and this behavior has been attributed to the...
lower rates of ROS production and the reduced vulnerability of bird tissue to ROS (8). In addition, birds typically have blood glucose concentrations that are two to four times higher than mammals (8), which again is consistent with their greater tolerance to oxidative stress (10).

These comparisons provide a hypothesis for the different evolutionary paths of avian and mammalian lungs. The argument is that the special properties of bird mitochondria conferred a selective advantage by allowing the avian gas-exchanging tissue to be exposed to the high oxygen partial pressure of the inspired air. This would have been especially true if the evolutionary paths began to diverge in the Carboniferous. By contrast, the more vulnerable gas-exchanging tissue in the mammalian lung required a lower PO2, and this was obtained by the reciprocating system of ventilation, which dilutes the inspired air with the resident alveolar gas. In other words, the reciprocating ventilation pattern of mammals protected the gas-exchanging tissue from the potentially damaging high inspired oxygen levels, but the penalty was a less efficient lung.

GRANTS
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DISCLOSURES
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REFERENCES