Review

Evolution and development of gas exchange structures in Mammalia: The placenta and the lung

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ABSTRACT

Appropriate oxygen supply is crucial for organisms. Here we examine the evolution of structures associated with the delivery of oxygen in the pre- and postnatal phases in mammals. There is an enormous structural and functional variability in the placenta that has facilitated the evolution of specialized reproductive strategies, such as precociality. In particular the cell layers separating fetal and maternal blood differ markedly: a non-invasive epitheliochorial placenta, which increases the diffusion distance, represents a derived state in ungulates. Rodents and their relatives have an invasive haemochorial placental type as optimum for the diffusion distance. In contrast, lung development is highly conserved and differences in the lungs of neonates can be explained by different developmental rates. Monotremes and marsupials have altricial stages with lungs at the early saccular phase, whereas newborn eutherians have lungs at the late saccular or alveolar phase. In conclusion, the evolution of exchange structures in the pre- and postnatal periods does not follow similar principles.

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1. Introduction: mammalian respiration organs and reproduction

The class Mammalia is divided into three groups, each characterized by their specific mode of reproduction: Monotremata are egg-laying, Marsupialia are characterized by the dominance of the yolk-sac placenta and in Eutheria chorioallantoic placentation is significant for fetomaternal exchange (Starck, 1975; Mossman, 1987). The associated reproductive strategies range from altricial neonates in ancestral mammals, monotremes, marsupials and the stem species of eutherians, towards intermediate and precocial forms that evolved in several eutherian taxa (Starck, 1975; Martin, 2003; Martin and McLarnon, 1985; see Novak, 1999 for data on the developmental conditions within mammals). An important aspect associated with the different reproductive strategies is the oxygen supply for the developing young and how this is facilitated in the pre- and postnatal phases. Primarily the placenta is providing oxygen for the fetus (Bartels, 1970; Schröder, 1995; Mess and Carter, 2006, 2007; Carter, 2009; Enders, 2009). In contrast to the lung, the placenta is a multi-functional organ; composed of the tissues of two individuals, with gas exchange representing only one of many functions (Enders, 2009). The gas exchange in the placenta is regarded to be less efficient than in the lung, because the minimum diffusion distance is larger and the permeability of the blood–blood barrier is lower than the permeability of the blood–gas barrier in the lung (Brandis, 2002). However, the intrauterine nourishment and placental gas exchange in mammals are efficient enough to enable different reproductive strategies. In particular, developmentally advanced fetuses require sufficient oxygen transfer across the placenta, whereas early stages tolerate anaerobic conditions—a fact that is regarded as a driving factor for the high degree of placental diversity in eutherians (Enders, 2009). After birth, the ability of the newborn animal to survive depends on the degree of maturation of the respiratory and circulatory systems. The newborn’s respiratory apparatus must be sufficiently developed to take over the gas exchange function previously provided by the placenta (Mortola, 2001). The various reproductive strategies of mammals – ranging from altricial to precocial – request different metabolic capacities of the animal. Compared to altricial newborns, which remain in a nest, precocial species need to have a high metabolic performance, necessary for active locomotion immediately after birth.

Thus the question arises if the evolution of the exchange structures in the pre- and postnatal periods follows recognizable principles. The null-hypothesis is that pre- and postnatal strategies for gas exchange are independent. Therefore, we tested the hypothesis that similar patterns are present throughout ontogeny. We provide the first combined analysis on the evolution of gas exchange structures during ontogeny in regard to the associated reproductive strategies.

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2. Methodological approaches

The improved understanding of mammalian interrelationships as revealed by molecular phylogenetics and other systematics stimulated attempts to trace patterns of organ evolution in regard to the placenta of Eutheria (e.g., Vogel, 2005; Mess and Carter, 2006, 2007; Wildman et al., 2006; Elliot and Crespi, 2009) or Marsupialia (Freyer et al., 2003) as well as for the lung development (Szdury and Zeller, 2009). Here we provide the first combined analysis on the evolution of gas exchange structures in the pre- and postnatal phases and their relevance for associated reproductive strategies. In order to compare evolutionary events during ontogeny, we plotted available data on one of the most comprehensive super-trees of Mammalia (Bininda-Emonds et al., 2007). Since the database is most restricted for lung development, we chose those families for analysis for which at least one species has been investigated in this respect (Table 1). In a second step data on the placenta were added. If no data were available for the originally chosen species, substitutions were done by using better investigated species (see Table 1).

We focused on the definitive placenta, i.e. near term of pregnancy, which marks the maximum potential for gas exchange and the developmental degree of the lung at birth. The data have been analysed by applying MacClade 4.0 (Maddison and Maddison, 2000) to the published tree topology (Fig. 1). The results are discussed in relation to the reproductive strategies with special reference to the developmental conditions of the newborn.

3. The placenta

A placenta is a structure for physiological exchange between mother and offspring (Starck, 1975; Mossman, 1987). It represents an interesting system of respiratory dynamics with a high degree of structural and physiological diversity (Mess and Carter, 2007). The mammalian placenta is derived from four extra-embryonic membranes evolved in amniotes: the amnion surrounding the embryo, the yolk sac and the allantois, which both could serve as a placenta in association with the chorion (Mossman, 1987; Mess et al., 2003). Umbilical vessels vascularized the chorioallantoic placenta, whereas vitelline vessels contribute to form a choriovitelline or yolk sac placenta. The chorioallantoic placenta, which acts as the main area for fetomaternal exchange in Eutheria (Mess and Carter, 2007), will be our primary frame of reference.

Several factors affect the oxygen transfer within the chorioallantoic placenta (e.g., Metcalfe et al., 1967; Bartels, 1970; Longo, 1987; Carter, 1989, 1999, 2009; Wilkening and Meschia, 1992; Schröder, 1995). However, physically gaining access to the placental complex for instrumentation is difficult and the evolutionary significance of this system is often not apparent. Most physiological features such as placental blood flow rates, hemoglobin concentration or blood oxygen affinity have continuous variables and do not allow tracing evolutionary trends (Carter, 2009). At present, morphology gives clues to factors with discontinuous variables, accessible for evolutionary analyses. Of special interest in this regard is the evolutionary history of the interhaemal barrier, i.e. the number of cell layers separating fetal and maternal blood (Mess and Carter, 2007; Carter, 2009). The interhaemal barrier is thought to influence the diffusion distance responsible for the oxygen diffusing capacity of the placenta (Carter, 2009). Originally recognized by Grosser (1909) and supported by electron microscopy, there are three principal types (Carter and Enders, 2004; Mess and Carter, 2006, 2007; Elliot and Crespi, 2009): in the epitheliochorial placenta the chorionic trophoblast is in contact with an intact uterine epithelium (Fig. 2A). In an endotheliochorial placenta the trophoblast is attached to the endothelium of the maternal capillaries because the uterine epithelium has been destroyed by the trophoblast (Fig. 2B). In a haemochorial placenta all the maternal tissues have been lost, including the capillary endothelium, and the maternal blood is directly in contact with the trophoblast (Fig. 2C). In contrast to quantitative or morphometric data (Baur, 1981; Mayhew, 2006), qualitative records including ultrastructural data are known for a broad cross-section of species.

Recent results indicate major evolutionary transformations within Eutheria. It has been shown that the last common ancestor of living Eutheria probably was characterized by endotheliochorial placentation (Vogel, 2005; Mess and Carter, 2006, 2007; Martin, 2008). An endotheliochorial placental type is also indicated by the present analysis based on a super tree (Fig. 1), but results may differ with a more complete taxon sampling (not done because of limited data on the lung). Other studies, differing in taxon sampling and using a range of statistical approaches for phylogenetic reconstructions, favor haemochorial placentation as ancestral for Eutheria (Wildman et al., 2006; Elliot and Crespi, 2009).

However, several transformations within the group have been indicated. There is broad agreement that a non-invasive epitheliochorial placenta represents a derived state in ungulates (Cetartiodactyla and Perissodactyla) and relatives (Vogel, 2005; Mess and Carter, 2006, 2007; Wildman et al., 2006; Klisch and Mess, 2007; Elliot and Crespi, 2009; Fig. 1). On the stem lineage to ungulates there was an evolutionary shift to precocial offspring. Even though the retention of an intact uterine epithelium increases the diffusion distance (Mess and Carter, 2006, 2007) an appropriate oxygen transfer must be provided. The perceived disadvantage of the epitheliochorial placenta for diffusion processes may have been countered by the increase in ambient oxygen during the Cenozoic era when large mammals radiated (see Mess and Carter, 2007). In ruminants the evolution of a cotyledonary placenta enlarges the exchange area by greater interdigitation of fetal and maternal tissues (Klisch and Mess, 2007). In contrast, rodents, lagomorphs and their relatives including humans possess the most invasive haemochorial placental type, representing the minimum number of layers as optimum for the diffusion distance (Mess, 2003; Vogel, 2005; Mess and Carter, 2006, 2009; Martin, 2008; Fig. 1). In particular, hystricognath rodents are characterized by numerous derived placental features. Transformations include a specialized placental architecture optimizing the area available for diffusion processes as judged from morphology, a fully countercurrent arrangement of the blood vessels, thinning of the trophoblast lining of the maternal blood spaces including surface extensions as well as a very effective mode of placental establishment and trophoblast invasion (Mess, 2001, 2003, 2007a,b,c,d). These evolutionary transformations on the stem lineage of Hystricognathi are thought to have positive effects on the oxygen supply of the fetus and certainly to contribute to their precocial reproductive strategy. In conclusion, the distinctive pattern of reproduction coincides with the successful radiation of hystricognaths (Mess et al., 2001; Mess, 2003).

Obviously, the enormous structural and functional plasticity of the chorioallantoic placenta enables the evolution of specialized reproductive strategies such as precociality in various ways. Indeed the placental types are associated with different developmental conditions: for instance, rodents possess a haemochorial type associated with either precocial or altricial strategies (Caviidae versus Muridae in Fig. 1). Endotheliochorial placentaion occurs in elephants characterized by precocial newborns, in shrews with altricial offspring as well as in tupids with intermediate forms (Fig. 1). The epitheliochorial placenta is associated mainly with precocial offspring as in ungulates (see Mess and Carter, 2006, 2007; Fig. 1), but also occurs in the American mole Sculpus with altricial reproduction (Carter, 2005). It is unlikely that transformations on the interhaemal barrier were driven by the respiratory need of the developing offspring only. In contrast, the evolution of the interhaemal barrier seems to be functionally associated with body mass (Elliot and Crespi, 2009). Moreover, divergent interests of mother
and offspring as well as conflicts between maternal and paternal genes may be responsible for the rapid evolution and diversification of fetomaternal interaction in the placenta (Haig, 1993; Zeh and Zeh, 2000; Crespi and Semeniuk, 2004; Elliot and Crespi, 2006). Functional support for non-invasive placentation may come from other systems, related to immunological factors, leading to stronger control of the mother which may benefit precociality (Moffett and Loke, 2006; Klisch and Mess, 2007).

Table 1
Lung development and placentation in mammals, chosen because of the availability of data on the lung. LD = lung developmental degree.

<table>
<thead>
<tr>
<th>Superorder</th>
<th>Family</th>
<th>Species</th>
<th>LD</th>
<th>Stage</th>
<th>Reference for the lung</th>
<th>Main references for placentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotremata</td>
<td>Tachyglossidae</td>
<td>Tachyglossus aculeatus</td>
<td>2 sa</td>
<td></td>
<td>Feren et al. (2009a)</td>
<td>Luckett (2007)</td>
</tr>
<tr>
<td></td>
<td>Ornithorhynchidae</td>
<td>Ornithorhynchus anatinus</td>
<td>2 sa</td>
<td></td>
<td>Feren et al. (2009a)</td>
<td>Luckett (2007)</td>
</tr>
<tr>
<td>Metatheria</td>
<td>Didelphidae</td>
<td>Marmosa robinsoni</td>
<td>2 sa</td>
<td></td>
<td>Barnes (1977)</td>
<td>Harder et al. (1993)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Didelphis virginiana</td>
<td>2 sa</td>
<td></td>
<td>Krause and Leeson (1975)</td>
<td>Zeller and Freyer (2001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dasyurus hallucatus</td>
<td>1 sa</td>
<td></td>
<td>Hughes and Hall (1988)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Macropus rufogriseus</td>
<td>3 sa</td>
<td></td>
<td>Walker and Gemmell (1983)</td>
<td></td>
</tr>
<tr>
<td>Phocidae</td>
<td>Phoca vitulina</td>
<td>S. crassicaudata</td>
<td>6 al</td>
<td></td>
<td>Boydien and Tompsett (1961)</td>
<td>Lee et al. (1983)</td>
</tr>
<tr>
<td>Otaridae</td>
<td>Zalophus californicus</td>
<td>E. arctos</td>
<td>6 al</td>
<td></td>
<td>Denison and Kooyman (1973)</td>
<td>Benirschke (2004a)</td>
</tr>
<tr>
<td>Odobenidae</td>
<td>Odobenus rosmarus</td>
<td>Amblyonx cinera</td>
<td>6 al</td>
<td></td>
<td>Denison and Kooyman (1973)</td>
<td>Benirschke (2004b)</td>
</tr>
<tr>
<td>Muridae</td>
<td>Mus musculus</td>
<td>E. rufus</td>
<td>4 sa</td>
<td></td>
<td>Ten Have-Opropaek (1980)</td>
<td>Kirby and Bradbury (1963) and Luckett (1985)</td>
</tr>
</tbody>
</table>

a No data.
b Substituted by another species belonging to the same genera or family, if placentation is not investigated for the original species, or member(s) of a genus for which data on placentation are available in case that lung development was studied in more than one species of a genus.

True chorioallantoic placentaion as established in Eutheria does not occur in other mammals: in the oviparous Monotremata an allantochorion provides fetomaternal exchange in the uterine phase but is covered by an egg shell and the shell membrane (Luckett, 1977; Fig. 1). In marsupials, an allantochorion in near term pregnancy is present only in some taxa such as wombats or peramelids (Mossman, 1987; Freyer et al., 2003). In the later, the fetal and the maternal parts are separated only by a thin epithelium
Evolution of structures associated with gas exchange in the pre- and postnatal phases in Mammalia. Data on lung development and placentation have been analysed by applying MacClade on a recently published super tree (Bininda-Emonds et al., 2007). Families were chosen for which at least one species has been investigated with respect to lung development. To include data on the placenta, substitution are necessary, e.g. Macroscelides has substituted by Elephantulus as has Zalophus by Amblonyx (see Table 1). Character conditions are given as numbers for the prenatal phase, respecting the chorioallantoic and the yolk sac placenta, and as colours on the tree for the lung differentiation at birth.

which may result by fusion of the fetal trophoblast with the uterine epithelium (epithelioendotheliochorial placenta: Mossman, 1987). The lack of a chorioallantoic placenta may be ancestrally for marsupials (Fig. 1). In contrast, a study with a broader taxon sampling than in the current analysis (without applying computer-aided modes of phylogenetic reconstruction) favors an allantochorion in the marsupial stem species pattern (Zeller and Freyer, 2001). However, all studies suffer from the limited data basis on marsupial placentation (Freyer et al., 2003).

Finally, yolk sac placentation differs among mammals (King and Enders, 1993; Fig. 1): in monotremes, the yolk sac provides fetomaternal exchange only via the egg shell and the shell membrane.

![Diagram of lung developmental degree in neonates](image1)

![Diagram of interhaemal barrier in the chorioallantoic placenta](image2)
The stem species pattern of Eutheria may be characterized by temporary yolk sac placentation (Mess and Carter, 2006; Fig. 1). In contrast, predominating yolk sac placentation represents an ancestral state for marsupials (Freyer et al., 2003; Fig. 1), through the shell coat in early pregnancy that is permeable for small molecules (Renfree, 1973, 1980). Separation between embryonic and trophoblastic areas of the blastocyst is distinct (Lillegraven, 2003), but the degree of invasiveness of this placenta differs: independent from the bilaminar or trilaminar part of the yolk sac, an invasive trophoblast resulted as ancestral for marsupials (Fig. 1). Similar to the degree of invasiveness of this placenta differs: independent from the bilaminar or trilaminar part of the yolk sac, an invasive trophoblast resulted as ancestral for marsupials (Fig. 1). Similar to the degree of invasiveness of this placenta differs: independent from the bilaminar or trilaminar part of the yolk sac, an invasive trophoblast resulted as ancestral for marsupials (Fig. 1).

4. The lung

During the prenatal period the fetus is well protected by the maternal uterus, in the postnatal period the offspring gets food in the form of milk and protection from the mother; finally after reaching sexual maturity the animal is able to care for itself. However, at birth the “decision” is made whether the organism is capable of surviving: that is, if all organ systems necessary for survival such as the cardio-respiratory system, the digestive system, and the brain are functioning and allow for extraterrestrial life. An essential organ in this context is the lung, because the survivability of the neonate depends to a great extent on the maturity of the respiratory apparatus.

The structural development of the mammalian lung is more or less the same in all mammals studied so far and occurs in several phases (Tschanz, 2007). In the embryological phase the respiratory diverticulum (lung bud) appears ventrally to the caudal portion of the foregut. As the lung bud grows, its distal end enlarges to form the tracheal bud, which divides into two primary bronchial buds that form the right and left main bronchi. During the pseudoglandular phase the entire conducting portion of the lung is formed and surfactant producing type II cells are already present. In the following canalicular phase small canaliculi appear at the endings of terminal bronchioles, they later form the lung parenchyma. Type II cells differentiate into type I cells, which form the blood–air barrier across which gas exchange occurs and capillaries penetrate into the lung parenchyma. These two processes are important to guarantee the extra-uterine function of the lung. During the saccular phase the lung parenchyma expands and smooth-walled saccules are formed at the ends of terminal bronchioles. Later, in the alveolar phase, the saccules transform into alveolar sacs with alveoli, the definitive structures for pulmonary gas exchange. The stage of lung development when mammals are born is quite variable, but not the chronology of final lung maturation. It always follows three consecutive steps: increase of lung volume by expansion of the airspaces, increase in lung tissue mass due to alveolization, and microvascular maturation (Burri, 1974; Zeltner and Burri, 1987).

In mammals there is a high variability in the degree of lung maturation at birth, reflecting the general development of the neonates (Engel, 1962). In the most immature neonates of monotremes and marsupials we find the earliest stage of lung development in which mammals are born: the lung structure is at the early saccular phase (Fig. 3A–C). The lung is composed of a primitive system of short branching airways which terminate in large terminal saccules providing only a small surface area, but they are sufficient for gas exchange. In monotremes, represented by the platypus (Ornithorhynchus anatinus), the saccules of the lung have a diameter of $320 \pm 13 \mu m$ (Ferner et al., 2009a; Fig. 3A). In marsupials there is a range in lung maturity, reflecting the general developmental degree of the different groups. Didelphids, represented by the grey short-tailed opossum (Monodelphis domestica), have large saccules of $453 \pm 22 \mu m$ in diameter, whereas the macropods, represented here by the tammar wallaby (Macropus eugenii), are characterized by saccules significantly smaller ($197 \pm 11 \mu m$) in size, and a more developed bronchial tree (Szdzuy et al., 2008; Fig. 3B and C).

Placental mammals have a wide range of developmental stages at birth, from altricial to precocial with many intermediate stages existing. The lung development ranges from the late saccular to the advanced alveolar phase (Szdzuy et al., 2008; Szdzuy and Zeller, 2009).

The lungs of altricial neonates, represented here by the golden hamster (Mesocricetus auratus), are at the late saccular stage of lung development (Fig. 3D). At birth the conducting airways occupy a large portion of the lung volume and the ramified bronchial tree extends far to the periphery of the lung. The saccules are numerous and small in size, they are measuring $96 \pm 3 \mu m$ in diameter in the golden hamster. An intermediate lung structure is presented by the Belangeri Tree shrew (Tupaia belangeri), the lung is at the transition between the saccular and the alveolar phase (Ferner et al., 2009b; Fig. 3E). Numerous small saccules as well as alveoli are present; the size of the airspaces is, with $47 \pm 2 \mu m$, half of that found in true altricial species. The most developed lung of all neonates can be found in precocial species, like the guinea pig (Cavia aperea). Here the lung is at the advanced alveolar stage (Fig. 3F). The lung parenchyma is highly subdivided and numerous alveoli and associated structures, such as respiratory bronchioles, alveolar ducts and alveolar sacs are already present, the airspaces have a diameter of around $28 \pm 1 \mu m$. As different as the lung structure in newborn mammals seems to be, a comparison of the lung in adult monotreme, marsupial and placental mammals shows that there are no major differences in the adult lung structure (Perry et al., 2000; Szdzuy et al., 2008). That means differences between the mammalian groups exist not in the final lung structure, but at the starting point and in the course of lung development.

Lung development in marsupials is generally slow. During the early postnatal lung development, the saccules become subdivided by septal crests and decrease in size. The first true alveoli, identified by the presence of single-capillary septa, are present at 28 days in the opossum and at 65 days in the tammar wallaby. A typical alveolized lung structure, characterized by the presence of respiratory bronchioles, alveolar ducts and alveolar sacs can be seen at 56 days in the opossum and at 142 days in the tammar wallaby. The postnatal lung development in altricial eutherians is much faster than in marsupial species. The first signs of the transformation from the saccular to the alveolar stage can be observed at 2 days after birth in the golden hamster and at the end of the first week a typical alveolized lung structure is present. Intermediate species, like the tree shrew, reach an alveolized lung structure within 4 days after birth and precocial eutherians are already born at this stage of development (Fig. 4).

The formation of alveoli and the associated microvascular maturation have an impact on the surface area of the lung. During this process the gas exchange surface area enlarges dramatically. In rats, the formation of alveoli occurs between days 4 and 10 after birth and results in a sharp rise in gas exchange surface area (Weibel, 1967). The alveolar surface increases by a factor of 2.6 during this short-time interval, from day 10 alveolar surface increases in relation to the gain of the body weight. This unusually steep growth rate of the alveolar surface area suggests that profound changes in pulmonary architecture must occur in the rat lung at this time, and indeed the microvascular maturation capillary surface area grows in close relation to the alveolar surface area (Burri et al., 1974). There is a large increase in pulmonary gas exchange area in utero associated with alveolar development in several precocial eutherian species (Alcorn et al., 1981; Hislop et al., 1984; Winkler and Cheville, 1985; Zeltner and Burri, 1987; Davies et al.,
Fig. 3. Light micrographs of the lungs of newborn O. anatinus (A), M. domestica (B), M. eugenii (C), M. auratus (D), T. belangeri (E) and C. aerea (F). The monotreme and marsupial lungs are at the early saccular phase with large saccules (A–C). The lungs of the altricial eutherian species are at the late saccular phase with numerous small sacculles (D), intermediate stages are born at the transition from saccular to alveolar phase (E), and the precocial eutherian species with respect to lung development are already at the advanced alveolar stage at birth (F). As, alveolar sac; b, bronchiole; bt, terminal bronchiole; br, respiratory bronchiole; sa, saccule. A, C, E, and F: Trichrome staining; B: Azan staining; D: HE staining.

Fig. 4. Time course of lung development in eight mammalian species. Monotremes (O. anatinus) and marsupials (M. domestica and M. eugenii) are born at the early saccular phase and have a slow postnatal lung development. Altricial eutherians (M. auratus and S. murinus) start at the late saccular phase and reach the alveolar phase soon after birth. Intermediate (T. belangeri) and precocial eutherians (C. aerea and M. proboscideus) are born at the early or advanced alveolar phase respectively.
1988; Castleman and Lay, 1990; Docimo et al., 1991). This suggests that the active precocial newborns, featuring high metabolic rates, require an advanced alveolar lung already at birth. The process of alveolization and the development of metabolic rate are linked, and the example of the tamar wallaby shows that exactly at the time at which alveolization begins – at around 65 days – the metabolic rate increases (Szdzuy, 2008).

A comparison of the monotreme, marsupial and placental lung structure shows that the mammalian lung is highly conserved and that the differences in the neonatal lungs can be explained by different developmental rates. The lung structure of newborn marsupials follows the general developmental degree at birth (Engel, 1962). Between the major taxa of marsupials we find a size variation of neonates in three different developmental degrees (G1–G3; Hughes and Hall, 1988). These size variations are paralleled by differing stages of lung development (Fig. 1). The smallest newborns of marsupials, the dasyurids (G1), have the most immature lungs with a small respiratory cavity, subdivided by a few simple partitions, superficially vascularised by respiratory capillaries. Most marsupial species, e.g. didelphids, peramelids and phalangerids (G2), have an intermediate size and lung development. Finally in the largest marsupial neonates, the macropodids (G3), the lung is greatly enlarged and highly subdivided by richly vascularised saccules. Also in eutherian mammals a correlation between general developmental degree and lung maturity is evident (Fig. 1). Typical altricial species, like shrews and mice-like rodents, are born at the late saccular phase of lung development with numerous small saccules. Intermediate species, like carnivores and tupaias, are born at the early alveolar phase. Finally precocial species, present in all mammalian superorders, are always associated with an advanced alveolar stage of lung development.

5. Conclusion

Since appropriate oxygen supply is crucial for the developing young, the evolution of structures responsible for gas exchange in the pre- and postnatal phases and their relevance for associated reproductive strategies have been reviewed under an organism view. An enormous structural and functional variability of the placenta enables the evolution of specialized reproductive strategies such as preocclusion by different ways: a non-invasive epitheliochorial placenta, which increases the diffusion distance, represents a derived state in ungulates. Rodents and relatives have an invasive haemochorial placental type as optimum for the diffusion distance. It is unlikely that transformations on the interhaemal barrier were driven by the respiratory need of the developing offspring only. The large range of placental functions as well as the divergent interests of mother and offspring may be responsible for the evolutionary plasticity of the placenta. In contrast, lung development is highly conserved and differences in the lungs of neonates can be explained by different developmental rates. Monotremes and marsupials are born at altricial stages with lungs at the early saccular phase, whereas newborn eutherians have lungs at the late saccular or alveolar phase. The correlation between the structural changes in the lung and the physiological implications suggest that the attainment of the alveolized lung has an impact on the metabolic developmental trajectory. This could be attributed to the surface area enlargement associated with this process. The metabolic development is linked to the structural differentiation of the lungs and the timing of postnatal lung development. In conclusion, the evolution of exchange structures of placenta and lung in the pre- and postnatal period follows independent principles, indicating that the null-hypothesis cannot be refuted. Evolution has not favored a particular placental-pulmonary combination for precocial or altricial mammals across phylogenetic lines. Most likely, the multi-functionality of the placenta with gas exchange as only one function and the specific role of the lung may explain the different evolutionary patterns of these organs.

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References

Denison, D.M., Kooyman, G.L., 1973. The structure and function of the small airways of the large range of placental functions as well as the divergent interests of mother and offspring may be responsible for the evolutionary plasticity of the placenta. In contrast, lung development is highly conserved and differences in the lungs of neonates can be explained by different developmental rates. Monotremes and marsupials are born at altricial stages with lungs at the early saccular phase, whereas newborn eutherians have lungs at the late saccular or alveolar phase. The correlation between the structural changes in the lung and the physiological implications suggest that the attainment of the alveolized lung has an impact on the metabolic developmental trajectory. This could be attributed to the surface area enlargement associated with this process. The metabolic development is linked to the structural differentiation of the lungs and the timing of postnatal lung development. In conclusion, the evolution of exchange structures of placenta and lung in the pre- and postnatal period follows independent principles, indicating that the null-hypothesis cannot be refuted. Evolution has not favored a particular placental-pulmonary combination for precocial or altricial mammals across phylogenetic lines. Most likely, the multi-functionality of the placenta with gas exchange as only one


