Ontogeny and allometry of metabolic rate and ventilation in the marsupial: Matching supply and demand from ectothermy to endothermy ☆

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ARTICLE INFO

ABSTRACT

The 'supply' of substrates should match 'demand' for energy utilization and not limit it. Integration of supply to demand would be expected to occur during ontogeny. As a result of a short gestation and protracted lactation most development in marsupials occurs *ex utero* in a thermally stable pouch, hence there is an early reliance on atmospheric oxygen. This paper explores through allometry the matching of ventilation (supply) and rate of oxygen consumption (demand) in the tammar wallaby from birth to adulthood, covering four orders of magnitude and the transition from ectothermy to endothermy. The allometric exponent for the scaling equation for the rate of oxygen consumption in the ectothermic and endothermic phases of development was 0.78, the difference in intercept between the two equations being approximately 2.5-fold. A similar exponent and factorial increase in intercept was found for ventilation. Hence, convective requirement is mass independent throughout development, from ectothermy to endothermy, being similar to previously published values for the class Mammalia. Altogether, these results support the notion that, at rest, supply by ventilation is matched to demand for oxygen during postnatal development in the marsupial.

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1. Introduction

Are animals designed so that the supply of substrates matches the demand set by the rate of energy utilization? Current arguments hinge on supply limitation models (see Banavar et al., 2002; West and Brown, 2005) versus multilevel regulation of metabolic scaling (see Suarez and Darveau, 2005). Issues surrounding metabolic state (e.g. basal or maximal), digestive state (e.g. can a post-absorptive state be achieved in a herbivore relying on fermentation, a suckling young?), body temperature and four dimensional biology (time) all undoubtedly influence the allometric exponent determined for metabolic rate (see Weibel et al., 2004; Weibel and Hoppeler, 2005; White and Seymour, 2004, 2005; West et al., 1999).

The presence of excess capacities in many physiological systems (Diamond, 1998), most notably studied in the cardio-respiratory systems of mammals (Weibel, 1987; Jones and Lindstedt, 1993) and reptiles (Frappell et al., 2002), demonstrates that the supply of substances to the cells would not be expected to limit metabolic rate. Excess capacity is contrary to the concept of symmorphosis, that has animals designed so that capacities match maximum loads (Taylor and Weibel, 1981). Nevertheless, symmorphosis also requires capacities in a multi-step pathway to be matched and this is consistent with the idea that allometry in capacities for the supply of substrates has been matched by allometry in capacities for energy utilization (Suarez et al 2004). Suarez and Darveau (2005) subsequently surmise that 'Supply and demand systems are better viewed as having coevolved with each other, as having developed as interacting systems during ontogeny, and as exerting acute regulatory influences upon each other in living animals'.

During its ontogeny the marsupial offers a unique opportunity to examine whether supply matches demand, at least in terms of oxygen delivery. As a result of a short gestation and protracted lactation most development in marsupials occurs *ex utero*, hence there is an early reliance on atmospheric oxygen. Indeed, it has been shown that in some very small newborn marsupials (dunnarts, genus *Sminthopsis*, birth weight ~12–17 mg) the lung serves no role in gas exchange at birth, instead the newborn is reliant entirely on cutaneous exchange of oxygen to meet its aerobic requirements (Mortola et al., 1999; Frappell and Mortola, 2000). In addition, marsupials are born ectothermic and the transition to endothermy occurs just prior to pouch vacation so that the young, once it vacates the pouch, is able to maintain adult body temperature (see Hulbert, 1988).

This paper explores the matching of resting ventilation (supply) and rate of oxygen consumption (demand) in the tammar wallaby (Macropodidae, *Macropus eugenii*) from birth, where there is approximately 30% reliance on cutaneous gas exchange (MacFarlane and Frappell, 2001), to adulthood, where the lungs are the sole gas exchange organ. The mass range from birth to adult covers four orders of magnitude and the transition from ectothermy to endothermy. Further, as for most macropods (kangaroos, wallabies and potoroids)

development of the ectothermic tammar wallaby young occurs in the confines of a warm and thermally stable pouch maintained at maternal body temperature (~36.5 °C). Subsequently, throughout development as the macropod transcends from ectothermy to endothermy, body temperature is maintained essentially constant (see Janssens and Rodgers, 1989). Use is made of this fact to remove the confounding effects that changes in body temperature may have on metabolic rate and hence scaling effects (see White and Seymour, 2005).

2. Materials and methods

The data presented were collected over a 15 year period and apart from a few individuals that formed parts of other studies have not previously been published. A total of 156 tammar wallabies (*Macropus eugenii*) from birth (~360 mg) to adulthood (~8 kg) comprising both sexes were measured for their rate of oxygen consumption ($\dot{V}o_2$), ventilation ($\dot{V}_E$) and breathing pattern at their normal body temperature (~36.5 °C); body temperature (T_b) and body mass (M_b) were measured immediately prior to measurement in all animals. The above measurements on post-pouch animals were made at adult thermoneutrality (ambient temperature 26–28 °C, Frappell and Baudinette, 1995) with the animal fully enclosed in a flow through respirometer. Small pouch young were either removed, weighed, fitted with a small face mask (see MacFarlane and Frappell, 2001) and enclosed in a water jacketed chamber at pouch temperature (~36.5 °C, unpublished observations and Janssens and Rogers, 1989) or, alternatively, the mother was sedated (3:1 alphaxalone/alphadolone
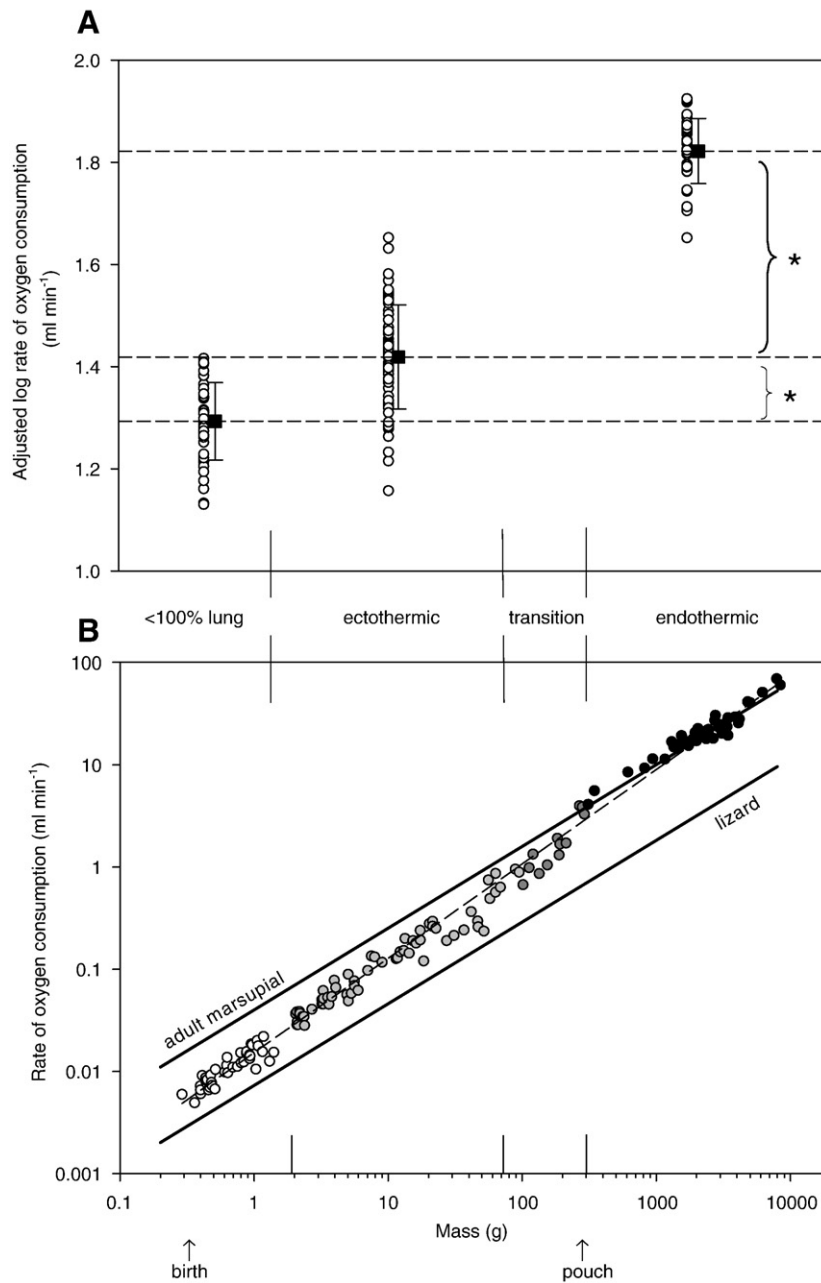

Fig. 1. Rate of oxygen consumption during postnatal development in the tammar wallaby. (A) Log adjusted values following standardisation of the covariate to the grand mean for each identifiable developmental age; ○ individual values, ■ mean value +/−1 S.E.M. (B) Rate of oxygen consumption as a function of mass. Prediction lines (solid) are indicated for resting lizards (Andrews and Pough, 1985) and adult marsupials (Frappell and Baudinette 1995), the dashed line is the overall regression for all the data; see Table 1 for actual regressions. Symbols are individual values, shading represents developmental stages: ○ <100% lung ◐ ectothermic, ◓ transition, and ● endothermic.

acetate, Saffan, Glaxovet, infused at a dose 0.75 mL kg^{-1} h^{-1}) and the young, while still attached to the teat, fitted with a face mask and placed in a water jacketed chamber set at pouch temperature. Given the amount of milk imbibed by a joey (Green, 1984) and the high metabolic clearance rate of Saffan (Flecknell, 1987), the effect of the drug on the joey at the given infusion rate was considered negligible. Larger pouch young, those capable of releasing and reattaching to the teat (approximate age 120 days), were treated like animals that had vacated the pouch. $\dot{V}o_2$ and $\dot{V}_E$ were, depending on the age of the animal, determined by methods previously described; in brief, for all animals (mask or chamber) $\dot{V}o_2$ was determined from the difference between incurrent and excurrent levels of oxygen after correcting for respiratory exchange ratio related errors (see Frappell et al., 1992 and Appendix A within). For masks, a pneumotachograph in the excurrent line measured flow associated with breathing. Integration of the flow trace yielded tidal volume (V_T) and together with breathing frequency (f_b) permitted determination of ventilation ($\dot{V}_E = V_T \times f_b$). For animals enclosed in an open flow respirometer $\dot{V}_E$ was determined by briefly sealing the chamber and the barometric method employed to determine tidal volume (see Frappell et al., 1992; Mortola and Frappell, 1998 for a critique of the method).

Values for $\dot{V}o_2$ are presented at STPD (273°K, 101.3 kPa, dry) and those for volumes at BTPS (body temperature, barometric pressure, saturated); the convective requirement ($\dot{V}_E/\dot{V}o_2$) is therefore not dimensionless. For determination of allometric equations the data were log–log transformed and for each variable a least-squares linear regression fitted to all the data and to defined developmental subsets (see Results). A test for homogeneity of slopes (ANCOVA) was conducted between the developmental stages for each variable. Where differences occurred, the common regression coefficient was computed and this was used to standardise the data for the covariate (log M_b in this case). Corrections for the covariate are normally made to the grand mean (see Packard and Boardman, 1999) but given the data in deriving allometric equations have been log–log transformed

and the exponent for each developmental stage for a variable is the same then proportionality across mass is maintained and adjustments were, therefore, made to a mass of 1 kg.

3. Results

3.1. Resting or basal metabolic rate

Before discussing the results, consideration should be given to the state of metabolic rate being actually measured. The values of metabolic rate (≡ rate of oxygen consumption) reported in this study were measured in individuals at rest and, when of endothermic age, at thermoneutrality. $\dot{V}o_2$ was measured, depending on age, for individuals still suckling, whether attached to the teat or young at foot, or in the herbivorous adult; no attempt was made to fast animals. Hence, values of $\dot{V}o_2$ reported in this study do not meet the rigid criteria of basal metabolic rate which is defined (see McNab, 1997; Frappell and Butler, 2004) as the minimal metabolic rate for a resting animal in the inactive phase of its circadian cycle, in steady state (i.e., no anabolic buildup of tissues—e.g., growth, fat storage, reproduction), and while post-absorptive (i.e., no digestion and assimilation costs).

3.2. Development of thermoregulatory ability

As has been previously documented in the tammar wallaby and other species of marsupials (Baudinette et al., 1988; Hulbert et al., 1991) the resting rate of oxygen consumption of newborn marsupials is close to that predicted for an adult lizard (ectotherm) of the same mass (Figs. 1 and 2). On first observations, $\dot{V}o_2$ would appear to gradually increase until it reaches that predicted for an adult marsupial of similar size, at about the time of pouch vacation (Fig. 1). Closer examination of mass-specific $\dot{V}o_2$ reveals that the ectothermic joey has a mass-specific $\dot{V}o_2$ slightly higher than that of a similar-sized lizard and that there is a clearly defined transition zone
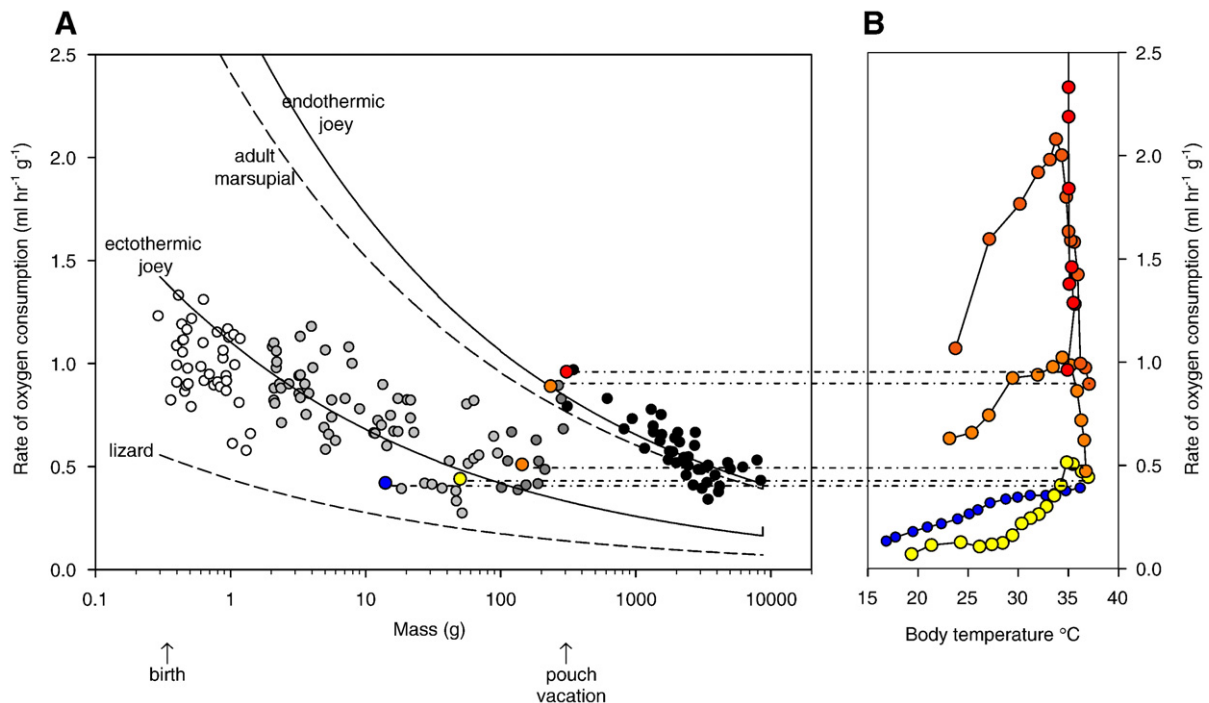

Fig. 2. Mass-specific rate of oxygen consumption in the tammar wallaby: (A) during postnatal development at a normal body temperature of 36.5 °C, symbol shading as for Fig. 1 and (B) in relation to body temperature, for given ages (indicated, coloured symbols), when exposed to changes in ambient temperature from 36.5 °C to 15 °C (S. Andrewartha and P. Frappell, unpublished). The data from B are projected to their appropriate mass (indicated by coloured symbols) in A and the transition from ectothermy to endothermy is considered to commence when the first thermogenic response to cold occurs (~70 g). The predicted relationships, indicated by lines, for resting lizards (Andrews and Pough, 1985) and adult marsupials (Frappell and Baudinette, 1995) are shown together with prediction lines for ectothermic and endothermic joeys (see Table 1).

between the 'ectothermic' and 'endothermic' phases of development (Fig. 2). This transition zone is well defined and corresponds to the period where thermoregulatory ability develops (Fig. 2), in the case of the tammar wallaby between postnatal days 55–200, which corresponds to a mass range of 70 g to 300 g.

3.3. Allometry

Across the entire mass range (360 mg to 8.4 kg) $\dot{V}o_2$ and $\dot{V}_E$ scale with similar exponents (=0.92, Fig. 3), V_T scales in direct proportion to mass and f_b with an exponent of −0.10 (Table 1). Over the course of development four developmental phases have been identified, including an early stage in which the joey is reliant to varying degrees on cutaneous gas exchange (see MacFarlane and Frappell,

2001); the early reliance on cutaneous gas exchange is also distinguished by break points in the relationships between f_b and V_T with mass (Fig. 4). For each variable, the exponents for the ectothermic and endothermic phases were similar (0.78), while that during the transition phase was higher. In addition, for $\dot{V}o_2$ and $\dot{V}_E$ the exponent in the early phase, where reliance to varying extent on cutaneous gas exchange still occurred, was the same as the ectothermic and endothermic phases (Table 1 and Fig. 4). Similar exponents for $\dot{V}_E$ and $\dot{V}o_2$ during the ectothermic and endothermic phases lend support to the notion that convective requirement ($\dot{V}_E/\dot{V}o_2$) is maintained throughout development (Table 1). Given similar exponents during the ectothermic and endothermic phases the average slope was calculated for each variable and the effect of mass removed by adjusting log values to a standardised log mass of

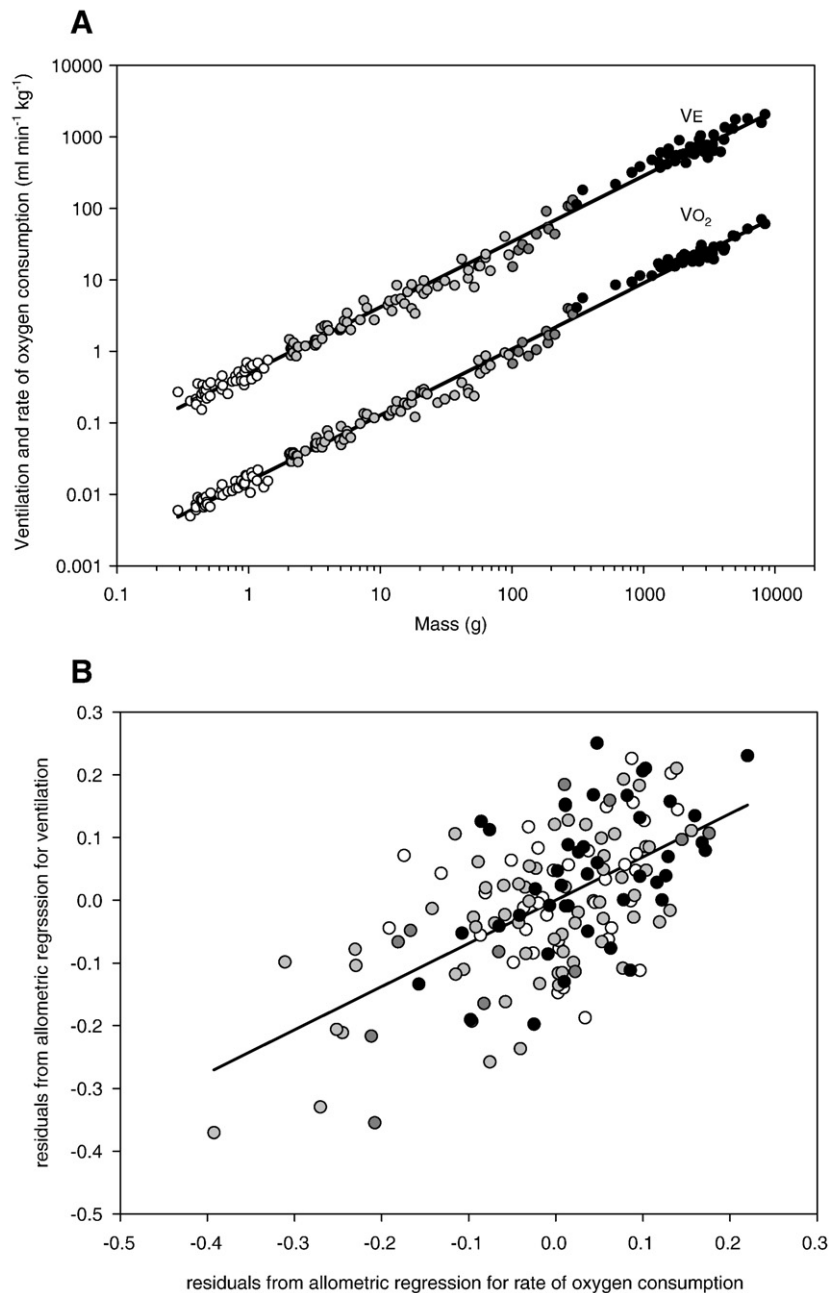**Fig. 3.** Rate of oxygen consumption and ventilation during postnatal development in the tammar wallaby. (A) The parallel lines represent the overall regression for each variable, details in Table 1. (B) After the effects of mass are removed with an analysis of residuals, there is a significant relationship (*P*=0.359) between ventilation and rate of oxygen consumption. Symbol shading as for Fig. 1.

Table 1
Allometric equations relating respiratory variables to mass in the tammar wallaby during postnatal development

	a	b	log a	S_a	S_b	S_{Y-X}	R^2
$\dot{V}o_2$ mL min^{-1}							
All	0.015	0.92[†]	−1.82	0.012	0.006	0.119	0.99
<100% lung	0.015	0.82[a†]	−1.82	0.017	0.068	0.076	0.77
Ectothermic	0.018	0.82[a†]	−1.74	0.028	0.025	0.101	0.95
Transition	0.001	1.54[†]	−3.17	0.442	0.197	0.074	0.84
Endothermic	0.066	0.75[a†]	−1.18	0.108	0.032	0.064	0.93
$\dot{V}_E$ mL min^{-1}							
All	0.501	0.92[†]	−0.30	0.014	0.007	0.119	0.99
<100% lung	0.501	0.83[b†]	−0.30	0.022	0.085	0.096	0.71
Ectothermic	0.589	0.82[b†]	−0.23	0.030	0.027	0.109	0.94
Transition	0.006	1.70[†]	−2.20	0.479	0.213	0.111	0.86
Endothermic	1.820	0.76[b†]	0.26	0.172	0.051	0.101	0.84
V_T mL							
All (lung only)	0.007	1.03[c]	−2.15	0.021	0.009	0.122	0.99
<100% lung	0.007	0.43	−2.18	0.021	0.080	0.090	0.42
Ectothermic	0.009	0.93[c]	−2.06	0.026	0.024	0.098	0.96
Transition	0.000	1.66	−3.63	0.813	0.362	0.188	0.65
Endothermic	0.012	0.96[c]	−1.91	0.188	0.056	0.110	0.88
f_b min^{-1}							
All (lung only)	66.07	−0.10[d]	1.82	0.018	0.008	0.102	0.57
<100% lung	75.86	0.39	1.88	0.013	0.052	0.059	0.57
Ectothermic	69.18	−0.12[d]	1.84	0.038	0.023	0.094	0.29
Transition	26.30	0.08	1.42	0.522	0.232	0.121	0.00
Endothermic	147.91	−0.20[d]	2.17	0.184	0.055	0.108	0.23
$\dot{V}_E/\dot{V}o_2$							
All	32.36	−0.01[‡]	1.51	0.012	0.006	0.101	0.00

Regression equations of the form log Y = log a + b·log M_b, where M_b is mass (g) and Y is any variable. Similar slopes between different developmental stages (see Fig. 2) for each variable are indicated by letters. [†] indicates slopes not significantly different between $\dot{V}o_2$ and $\dot{V}_E$ for same developmental stages. [‡] indicates slope not significantly different from zero. No difference existed for $\dot{V}_E/\dot{V}o_2$ between developmental stages in intercept or slope, equation only presented for All. N = 156 for All, N = 116 for All (lung only), N = 40, 62, 12 and 42 respectively for subsets: <100% lung (<2 g), ectothermic (2–70 g), transition (70–300 g) and endothermic (>300 g). S_a and S_b are the standard errors of the intercept (a) and the slope (b), respectively; S_{Y-X} is the standard error of the estimate; see text for other abbreviations. In all cases a significant difference is defined as P < 0.05.

1 kg (Table 2, Fig. 1). Analysis of adjusted values revealed for $\dot{V}o_2$ and $\dot{V}_E$ similar slopes and a factorial change of approximately 2.5 between ectothermic and endothermic levels. For $\dot{V}_E/\dot{V}o_2$ the average slope was not significantly different from zero and there was no factorial change (Table 2). Analysis of residuals from the allometric relationships for $\dot{V}_E$ and $\dot{V}o_2$ reveals a positive correlation (Fig. 3). In the case of V_T and f_b the factorial change was 1.64 and 1.42, respectively (Table 2).

4. Discussion

The allometric exponents are typical of those reported in marsupials in general (see Frappell and Baudinette, 1995), with the rate of oxygen consumption and ventilation scaling with similar exponents close to 0.80, tidal volume in direct proportion to mass and breathing frequency with an exponent of −0.16. These exponents are close to the basic design rules of scaling across phylogenies in air breathing vertebrates, where volumes scale linearly with mass, rates (the reciprocal of time) with an exponent of −0.25 and volume rates (such as $\dot{V}_E$ and $\dot{V}o_2$) scale with an exponent of 0.75 (see Stahl, 1967; Calder, 1984; Frappell and Baudinette, 1995; Frappell et al., 2001; Lindstedt and Schaeffer, 2002). The coefficient of the allometric equation for convective requirement is similar to that previously reported in mammals (Frappell and Baudinette, 1995).

4.1. Ectothermy versus endothermy

As previously shown (Baudinette et al., 1988; Geiser et al., 1986; Hulbert, 1988; Shield, 1966) the resting rate of oxygen consumption of marsupial pouch young during the early stages of pouch life is close to that predicted for an ectotherm of similar size. $\dot{V}o_2$ gradually increases during development until just prior to pouch vacation where it reaches endothermic levels (Baudinette et al., 1988; Farber et al., 1972; Geiser et al., 1986; Hulbert, 1988; Petajan and Morrison, 1962; Shield, 1966). It was noted for eutherians by Brody (1974), and subsequently by Weiser (1984), that following birth and during the period of rapid growth that the allometric exponent is close to unity. After a critical age, not necessarily related to weaning or sexual maturity, there is general slowing in the allometric growth of metabolism. Indeed, Weiser (1984) notes that this stage is the longest part of an animal's life span, that it is accompanied by little structural change and that the allometric exponent is close to 2/3 (see West and Brown, 2005; Suarez and Darveau, 2005; White et al., 2007 for debate about the value of the allometric exponent relating metabolic rate to body mass).

In this study, the ectothermic and endothermic levels of metabolism in the developing marsupial do not differ in their allometric exponents (on average 0.78, which is close to the 3/4 scaling). Because rates of cellular metabolism scale allometrically (reviewed by Suarez et al., 2004; though see West et al., 2002 and Brown et al., 2007 and the refutation by Wheatley, 2007) the finding of similar allometric exponents between the ectothermic and endothermic phase of ontogeny in the marsupial is not surprising. Endotherms, generally, are characterised by cells with greater mitochondrial volume, membrane densities and leakier membranes and an associated approximately sevenfold increase in cellular metabolism that maintains higher ion and proton fluxes for a given body temperature (see Else and Hulbert, 1981, 1987; Else et al., 2004 and references within). The sevenfold difference in cellular metabolism is reflected in the rate of oxygen consumption for the whole organism. In contrast, the difference between the ecto- and endothermic phases of development in the tammar wallaby was of the order of 2.5-fold. This probably reflects the fact that during the ectothermic phase $\dot{V}o_2$ for a given mass was higher than reported for a typical lizard (ectotherm) and that the adult marsupial has a metabolic rate somewhat lower than an adult eutherian.

Interestingly, a recent meta-analysis reported ectotherms as having a scaling exponent greater than 3/4 whereas the endotherm exponent was between 2/3 and 3/4 (White et al., 2007) While this study did not reveal a significant difference between the ectothermic and endothermic phases of development in the marsupial there was a tendency for the ectothermic phase to have a greater exponent (see Table 1).

During the transition period the exponent is (obviously) much greater than unity as metabolic rate is up-regulated towards endothermic levels, presumably due to changes in mitochondrial membrane properties and the associated increase in obligatory thermogenesis (see Else et al., 2004; Frappell and Butler, 2004). Identification of steeper metabolic scaling exponents during development is not new. Increased metabolic scaling during ontogeny is associated with the costs of growth and development in a range of taxa, whereas in endotherms an exponent greater than unity has been attributed to the escalating costs associated with the development of endothermy (see extensive review by Glazier, 2005 and references within). Another view, is that in marsupials, at least the tammar wallaby, the metabolic development of different tissues has different timetables and so the actual allometric exponent during the transition period may be an empirical artefact and not necessarily have any underlying physiological basis (Hulbert et al., 1991). However, the finding of tissues with different timetables is not all that different from the views of Darveau et al. (2002) who note that metabolic rate represents the sum of tissue metabolic rates and that the proportion each tissue contributes can be adjusted depending on the circumstances (e.g. rest versus exercise). During the transition period from ectothermy to endothermy in the tammar, emphasis is placed on the up-regulation of thermogenic capability and regulation of Tb which by
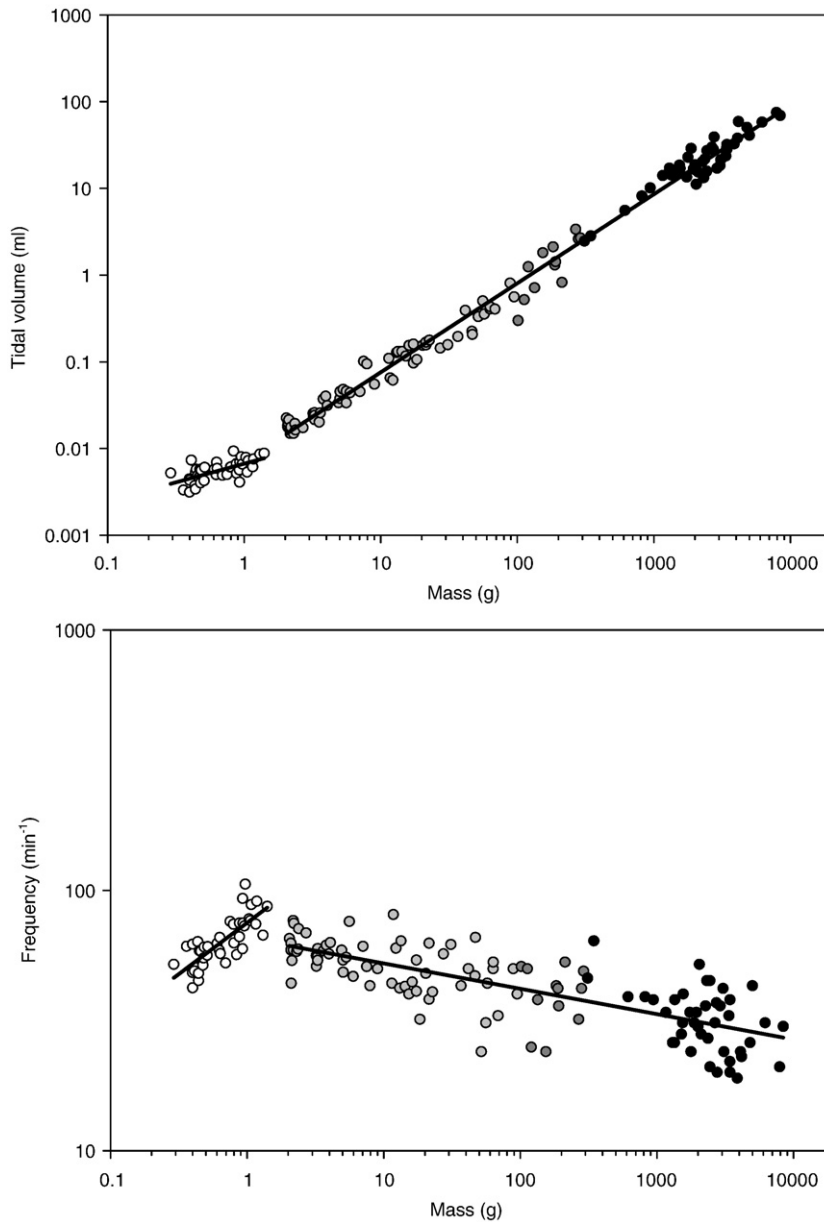
Fig. 4. Tidal volume and breathing frequency during postnatal development in the tammar wallaby. Regression lines (see Table 1) have been fitted to the data, pre- and post-break points observed which correspond to the point where cutaneous gas exchange becomes of minor importance (see MacFarlane and Frappell, 2001). Symbol shading as for Fig. 1.

virtue of the large increase in heat required would see the metabolic scaling exponent increase. Associated with increased metabolic scaling during the transition period is the attainment of well-developed alveoli, ensuring that gas exchange is not limited by surface area (Frappell and MacFarlane, 2006).

4.2. Supply and demand

MacFarlane and Frappell (2001) noted in the early neonatal tammar wallaby that the convective requirement was established at a value similar to that observed in the adult. The present study confirms that

Table 2
Values for respiratory variables following the removal of the effect of mass and the factorial change associated with the transition from ectothermy to endothermy

		Average slope	Ectothermic	Endothermic	P	Factorial change
$\dot{V}_{O_2}$	mL min^{-1}	0.780	0.639±0.102 (4.35)	1.042±0.064 (11.00)	<0.001	2.53
$\dot{V}_E$	mL min^{-1}	0.790	2.167±0.109 (147)	2.534±0.099 (342)	<0.001	2.33
V_T	mL	0.949	0.768±0.097 (5.86)	0.982±0.109 (9.59)	<0.001	1.64
f_b	min^{-1}	−0.160	1.401±0.095 (25.2)	1.552±0.107 (35.7)	<0.001	1.42
$\dot{V}_E/\dot{V}_{O_2}$		0.009	1.489±0.101 (30.8)	1.498±0.098 (31.5)	0.662	1.02

Logarithmic values have been adjusted to a log mass of 1 kg using the average slope determined following a test for homogeneity of slopes (ANCOVA) between the allometric equations calculated for 'ectothermic' and 'endothermic' tammar wallabies (see Table 1).
Values are logarithmic values, mean±1 S.E.M. Values in parentheses are anti-logarithms. P indicates the level of significance following ANOVA on adjusted values.

finding and further shows that convective requirement is maintained throughout development. Hence, the 'blueprint' that ensures supply matches demand is established early in development in the marsupial and maintained through the transition to endothermy.

Maintaining a match between supply and demand across body sizes clearly requires that both processes, in this case ventilation and the rate of oxygen consumption, to scale with body mass in the same manner. If this were not true then a mismatch between supply and demand would occur, resulting in inefficiencies. Nevertheless, some degree of mismatch between exponents can be maintained if other physiological processes were able to compensate (Banavar et al., 2002). While it would be wasteful for supply rate to exceed the rate of demand, such excess capacity does permit a degree of safety under conditions where the system is made to operate maximally (see Diamond, 1998).

An increase in the rate of oxygen consumption and an accompanying increase in ventilation has been previously demonstrated during development in other endotherms (e.g. rats, Mortola et al., 1994), though not across as many orders of magnitude or with such a marked transitional increase in metabolic rate. It is not unusual for large increases in the rate of oxygen consumption, such as it occurs during exercise or thermogenesis (e.g. Newstead, 1987) to be accompanied by parallel increases in ventilation. Maintenance of the convective requirement makes sense from the perspective of ensuring consistency of alveolar, hence arterial blood gases, as dictated by the alveolar gas equations. The pH of blood is related to the transport of CO_2 (Henderson–Hasselbach equation) and consistency of the arterial partial pressure of CO_2 throughout development, coupled with constant body temperature, should ensure stability of blood pH, permitting optimum enzyme function and reducing the need for a suite of isozymes with differing optimal temperatures and/or pH ranges.

5. Conclusion

Marsupial development is characterised by extended *ex utero* development of a small altricial young in the confines of a warm and thermally stable pouch. During development the young transitions from being ectothermic to endothermic. Both phases are characterised by similar allometric exponents for the rate of oxygen consumption and ventilation, hence convective requirement is maintained despite a 2.5-fold increase in metabolic rate due to endothermy. Not only is demand matched by supply but maintenance of the convective requirement ensures consistency of the arterial blood gases, that coupled with a constant body temperature throughout development will ensure stability of blood pH. Overall, these findings support the concept that supply and demand systems are integrated under resting conditions to ensure that demand is not limited at any time during development.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.cbpa.2008.02.017.

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