Scaling of respiratory variables in mammals

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Stahl, Walter R. Scaling of respiratory variables in mammals. J. Appl. Physiol. 22(3): 453-460. 1967.—Data have been collected from the literature on respiratory variables and correlated against body weight on the assumption of log-log relationships (allometry) with the use of computer regression analysis. Statistically validated power law formulas, with correlation coefficients of 0.99-0.90, are presented for lung weight, VC, TLC, FRC, VT, VO₂, VO₂, f, Cl, Dlco, Dlo₂, total respiratory flow resistance, work per breath, and several nonrespiratory parameters. The study deals principally with the rat-human size range, but the prediction formulas probably cover mice to steer and possibly all mammals. Predicted and observed values are compared for the rat, cat, dog, and man; good agreement is demonstrated. Size-independent dimensionless and dimensional respiratory invariants or “design parameters” may be obtained by forming simple and complex quotients from the individual power laws that have net residual mass exponents (dependency on body weight) approaching zero.

respiratory scaling laws; respiratory allometry; body size and respiratory variables; respiratory dimensional constants

Mammals occur in the size range of 2.5-g shrews to 150-metric-ton blue whales, which represents a weight increase of roughly 70 million. In spite of this enormous variation in weight the heart, lungs, kidneys and other major organs of mammals show much similarity in morphology and function. The 1- to 2-g heart of a rat and 100-kg heart of a medium-sized whale look surprisingly alike except for size. Integrated scaling of physical variables is a necessity for function of the mammalian system over any substantial changes in body weight. This study deals with the scaling laws or power law prediction formulas for basic respiratory variables.

In a series of previous reports the author (54, 57) explored the application of engineering dimensional analysis or physical analogue theory in physiology. By canceling statistically fitted power law prediction formulas for various physiological parameters it is possible to obtain dimensional constants and dimensionless “design criteria” which characterize integrated mammalian physiology. It follows that lungs in small and large mammals are physically similar systems or physical analogues of each other, as this concept is used in dimensional analysis theory. The reduction of data to size-independent form also makes possible the systematic comparison of respiratory function in different sizes and species of mammals.

METHODS

Data were collected from standard physiological journals, handbooks, etc., checked for units consistency and general validity, and key punched for computer processing. Handbooks examined include those edited by Spector (27), Dittmer and Grebe (3), Altman and Dittmer (7, 8), and Fenn and Rahn (22, 23). Major sets of comparative respiratory data are provided by Crosfill and Widdicombe (17), Agostoni, Thimm, and Fenn (2), and Radford (50). Power law formulas for respiratory parameters have been discussed previously by Brody (10), Adolph (1), Guyton (25), Gunther and Guerra (24), Drorbaugh (18), Bartels (5), Kleinman and Radford (34), and Tenney and Remmers (59). Specific reports were also used, containing data on the rat (38, 39, 43), cat (6, 11, 19, 22, 31, 37, 44-46, 52), dog (3, 12, 13, 15, 29, 35, 36, 40, 41, 49, 53, 58), goats and sheep (3, 4, 26), and steer and horses (10, 23). Normal human values are given by Comroe et al. (14). The majority of data points are from a comparatively small number of reports by experienced respiratory physiologists who did repeated determinations on groups of animals.

Statistical analysis was performed on a SDS-920 computer (with the assistance of D. L. Lindgren and D. Williams). The data were transformed to base 10 logs and then fitted by a conventional least-squares regression analysis, to yield the parameters in the “allometric” formula \( x = aM^b \), with \( x \) any variable and \( M \) mass or body weight in kilograms. The parameter \( a \) is the actual value of the variable for a 1-kg “standard animal” while \( b \) is the slope on a log-log graph. The most informative statistical measures were taken to be the correlation coefficient (\( r \)), 95 % confidence limits for
repeated lines fits ($s_a$ and $s_b$), and the standard error of the estimate ($S_a$), which has much the same significance for a regression line as a standard deviation for a mean, i.e., $2S_a$ limits should include 95% of cases. With log-log analysis $+S_a$ and $-S_a$ differ slightly (see figures); a mean of the two values is shown in the tables for purposes of simplicity.

As seen from Table 1, over 250 data points were found for many variables, with greater than 600 for tidal volume, minute volume, and blood volume. In order to prevent excessive bias towards human values the generally accepted means for humans were weighted as 20-50 data points, depending on the total number of nonhuman values. The number of data points, $N$, shown in Table 1 is the summation of individual measurements plus one-half of the number of determinations entering mean values used in the correlation. This is an arbitrary but conservative means for summing means and single data values; more complex statistical techniques were not attempted because necessary statistics are not given with most published means. A computer program was also written for predicting expected ranges of variables from the values and standard errors of the $a$ and $b$ coefficients.

### RESULTS

Table 1 presents the power law (allometric) coefficients for respiratory variables. Figs. 1-4 are representative graphs of the data which demonstrate that the line fits are generally satisfactory. The data in Table 1 are notable for high $r$ values and narrow 95% confidence limits ($s_a$ and $s_b$), even in the case of variables on which there is limited data, e.g., $DL_{TQ}$.

Table 2 contains systematic predictions of 10 respiratory variables for the rat, cat, dog, and man. The value shown is a range based on simultaneous 1 standard error limits of the $a$ and $b$ coefficients. This table reveals surprisingly good agreement of predicted and observed values; even better results can be obtained if the specific weights of animals are used in the formulas rather than an over-all mean species figure. It should be noted that for an individual species such as the cat or dog the experimental results often differ among themselves by 100% or more because of experimental error or animal variations. The formulas also give reasonable order of magnitude estimates for basic respiratory variables in kangaroos (42) and giraffes (51), although these animals are probably too specialized to fit precisely on the "normal mammalian" prediction lines. Good results have also been obtained in prediction of values in the rhesus monkey. Studies on smaller groups of animals and during growth of individual species often give less satisfactory correlations; the power laws arising in maturation are usually not the same as, but comparable to, those found in adult size-change comparisons.

The validity of the computed power law formulas is also confirmed by comparisons with previously published estimates of respiratory allometric coefficients, such as those of Guyton (25), Drorbaugh (18), and Tenney and Remmers (59). For example, in a report from 1947 Guyton found $VT$ (ml) = 7.4 $M^{.88}$, while the new value is $VT$ (ml) = 7.69 $M^{.88}$; Drorbaugh (18) obtained $VC$ (ml) = 63 $M^{.88}$, with the new formula; $VC$ (ml) = 56.7 $M^{.88}$. This author also reported a formula for compliance (ml/cm H2O) = 1.21 $M^{.88}$; Table 1 yields the formula, compliance (ml/cm H2O) = 1.56 $M^{.88}$. The prior allometric estimates were given without necessary statistical limits, but the old and new regression formulas agree within ±10% in several cases.

Tables 3 and 4 illustrate what the author (54-56) has called the "allometric cancellation" technique and applied to a wide variety of physiological and somatic allometric prediction formulas. Consider, for example, the power laws $VC$ (ml) = 56.7 $M^{.88}$ and blood volume (ml) = 65.6 $M^{.03}$ ($M$ in kg), which were computed independently using 315 and 840 data points, respectively. The quotient:

### TABLE 1. Power law prediction parameters for respiratory variables in mammals*

<table>
<thead>
<tr>
<th>Variable, Units</th>
<th>$a$</th>
<th>$b$</th>
<th>$r$</th>
<th>$N$</th>
<th>$s_a$</th>
<th>$s_b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lung wt, g†</td>
<td>11.3</td>
<td>0.96</td>
<td>0.96</td>
<td>&gt;100 ~ 15</td>
<td>50.0 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>Total lung cap, ml</td>
<td>53.5</td>
<td>1.06</td>
<td>0.08</td>
<td>300</td>
<td>40.0 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>Vital cap, ml</td>
<td>39.7</td>
<td>1.03</td>
<td>0.09</td>
<td>315</td>
<td>19.0 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>Funct resid cap, ml</td>
<td>34.3</td>
<td>1.03</td>
<td>0.07</td>
<td>264</td>
<td>45.0 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>Tidal vol, ml</td>
<td>2.76</td>
<td>0.96</td>
<td>0.05</td>
<td>264</td>
<td>42.0 ± 0.09</td>
<td></td>
</tr>
<tr>
<td>Resp rate, min⁻¹</td>
<td>35.3</td>
<td>-0.46</td>
<td>-0.91</td>
<td>662</td>
<td>40.0 ± 0.01</td>
<td></td>
</tr>
<tr>
<td>Minute vol ml/min</td>
<td>379</td>
<td>0.86</td>
<td>0.98</td>
<td>661</td>
<td>45.0 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>Oxygen uptake, ml/min</td>
<td>11.6</td>
<td>0.76</td>
<td>0.98</td>
<td>349</td>
<td>30.0 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>Lung compliance, ml/cm H2O</td>
<td>2.16</td>
<td>1.0</td>
<td>0.98</td>
<td>306</td>
<td>32.0 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>Thoracic compliance, ml/cm H2O</td>
<td>4.52</td>
<td>0.86</td>
<td>0.98</td>
<td>306</td>
<td>38.0 ± 0.05</td>
<td></td>
</tr>
<tr>
<td>Total compliance, ml/cm H2O</td>
<td>1.39</td>
<td>1.04</td>
<td>0.99</td>
<td>314</td>
<td>36.0 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>Total airway resit., cm H2O/liter/see</td>
<td>24.4</td>
<td>-0.5</td>
<td>-0.6</td>
<td>137</td>
<td>38.0 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>Work/breath, gm/cm</td>
<td>17.1</td>
<td>0.58</td>
<td>0.96</td>
<td>68</td>
<td>47.0 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>Power of breathing, gm/min</td>
<td>662</td>
<td>0.78</td>
<td>0.98</td>
<td>89</td>
<td>49.0 ± 0.03</td>
<td></td>
</tr>
<tr>
<td>Diffusing cap CO2, ml/min per mm Hg</td>
<td>0.22</td>
<td>1.14</td>
<td>0.96</td>
<td>238</td>
<td>44.0 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>Diffusing cap O2, ml/min per mm Hg</td>
<td>0.16</td>
<td>1.18</td>
<td>0.98</td>
<td>238</td>
<td>21.0 ± 0.05</td>
<td></td>
</tr>
<tr>
<td>Total blood vol, ml</td>
<td>65.6</td>
<td>1.02</td>
<td>0.95</td>
<td>840</td>
<td>34.0 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>Heart wt, g‡</td>
<td>5.8</td>
<td>0.98</td>
<td>0.96</td>
<td>&gt;200 ~ 15</td>
<td>41.0 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>Cardiac output, ml/min</td>
<td>107</td>
<td>0.91</td>
<td>0.98</td>
<td>308</td>
<td>31.0 ± 0.01</td>
<td></td>
</tr>
<tr>
<td>Cardiac rate, min⁻¹</td>
<td>24.1</td>
<td>-0.25</td>
<td>-0.88</td>
<td>447</td>
<td>34.0 ± 0.02</td>
<td></td>
</tr>
<tr>
<td>Body area, n²</td>
<td>0.11</td>
<td>0.63</td>
<td>0.95</td>
<td>&gt;100 ~ 20 ~ 30.0 ± 0.04</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Statistical fit of $y = aX^b$, $M$ in kg; $r =$ correlation coefficient; $N =$ total data points; $s_a =$ 95% confidence limits of $a$ in percent; $s_b =$ 95% confidence limits of the estimate of $a$ in percent; $S_a =$ 95% confidence limits on $b$ in slope units from mean slope value.
† Modified from Brody (10). ‡ From Stahl (59).
allometric analysis of respiratory variables in mammals

**Figure 1.** Allometry of total lung capacity in mammals from the mouse to cattle and steer. Most of the points are mean values. Dashed lines indicate standard error of the estimate.

**Figure 2.** Allometry of lung compliance. The larger points are often mean values, with smaller ones individual measurements from a variety of reports. The dashed lines indicate standard error of the estimate.

Vital capacity = \(56.7 M^{1.03}\) blood volume = \(65.6 M^{0.62}\) residual mass index (RMI) of only 0.001 slope units, which is not different from zero on the basis of the statistical slope limits for VC and BV given in Table 1. Any number to the zero power equals unity, so for all values of \(M\) in kilograms the VC/BV ratio is invariant of size on the basis of available data. The expected accuracy of the quotients in Tables 3 and 4 depends on
Fig. 3. Allometry of carbon monoxide diffusing capacity. Most of the points are individual determinations for the cat, dog, and man, from sources cited in the text. The dashed lines indicate ± standard error of the estimate.

\[ D_{L-Co} = 0.22M^{0.94} \]

\[ (n=258, r=0.96) \]

Fig. 4. Allometry of lung weight. The data points are for primates ranging in size from about 0.2 to 100 kg, with some data also on the tree shrew, which is an insectivore related to primates. The line previously computed for mammals in the mouse-elephant range near overlaps the new one for primates. From Stahl (56), which gives citation for additional sources shown on figure.

The standard errors of their components and is approximately ±15 to ±50 for various constants. The last two entries in Table 4 are composed of three variables, yielding dimensionless group with RMI's of -0.02 and 0.08, respectively, both within statistical limits of zero.

For respiratory variables RMI values below 0.08 are probably not significant but several values above 0.08 in Tables 3 and 4 suggest a systematic small "size effect" on the dimensional constant or dimensionless proportion in question. For example, DLco per unit of lung weight...
The power law quotient for this variable is 32.7 with a RMI of —0.08, which is probably not significant.

An inulin for human beings or laboratory mammals (34), an inine (Vd/Vt) ratio of 0.3-0.4 is usually cited as significant. In neonates (2), the ratio Ve/Vo2 is sometimes called the "ventilation efficiency" and has a normal value for humans (14) of about 13%, which is in reasonable agreement with reported data. The value of Ve/Q is 2.03 (RMI = —0.01); figures of 1.0-2.0 are typical for human beings.

The same technique may be applied to more complex variables. The ratio of lung compliance over VC has a mean value of 0.037 (cm H2O)-1 or 37 ml/cm H2O per liter (RMI = 0.06). Agostoni, Thimm, and Fenn (2) found 28-39 ml/cm H2O per liter in a rat, cat, dog, and man series. Table 3 shows lung compliance per gram lung to be 0.18 ml/cm H2O per g (RMI = 0.99). Crosfill and Widdicombe (17) report figures of 0.2-0.7 ml/cm H2O per g in a mouse-man series. Cook, Helliesen, and Agathon (15) found quite similar values in growing children, though ordinarily it cannot be assumed that the scaling laws and constants obtained from adult mammalian comparisons will apply precisely to maturation data. In studies on dogs, Collier and Mead (13) normalized total compliance by body weight, obtaining figures of 1.6 ml/cm H2O per g. The predicted value is 1.56 ml/cm H2O per kg (RMI = 0.04). However, there are no known prior estimates of the scaling laws for diffusing capacity. The observed somatic indices of Dlco and Dl0 are in good agreement, suggesting that the somatic index of Dl is distinctly above unity; predictions for specific animals in Table 2 are in reasonable agreement with measurements. Table 3 shows Dlco/TLC to be 0.0041 ml/mm Hg per min per ml with a RMI of 0.08, which implies that Dl scales more closely as TLC than lung weight. In a study of cats, Lawson et al. (37) include data that makes Dlco/TLC equal 0.0039 ml/mm Hg per min per ml, while figures...
for dogs from Burrows and Niden (12) are 0.004-0.014 ml/mm Hg per min per ml. In his thorough analysis of diffusing capacity in human beings, Forster (21) finds $D_{LCO}$ values of 0.0035 ml/mm Hg per min per ml. Rosenberg and Forster (52) normalized $D_{LCO}$ by lung weight; their data (converted from dry to wet lung weight) are equivalent to 0.015-0.027 ml/mm Hg per min per g, while the predicted value of this parameter from Table 3 is 0.019 ml/mm Hg per min per g.

The final two entries in Table 4 each contain three component power formulas, but nonetheless have RMM’s of -0.02 and 0.08, respectively, which is a rather impressive reduction of complex data, which is otherwise confirmed by the tautology $V = V t \times f$ and should be unity by definition; the deduced value of the quotient is 1.06, within statistical limits of 1.00. This relationship was also shown in 1947 by Guyton (25). The second entry, namely, CLR/respiratory period, with Ct and R in consistent units, may be understood as a ratio of a relaxation time (comparable to RC of electric circuit theory) to an actual period time. The low value of 0.034 is not surprising when it is noted that inspiration or expiration occupies only a portion of the breath cycle at rest and also that breathing rate may rise by 3-4 times. At maximal rate the ratio of relaxation time to inspiration or expiration time would be much closer to unity. Crossfill and Widdicombe (17) obtained values for the RC relaxation time in individual animals; log-log plotting of their data gives a somatic index in the range 0.25-0.33, in agreement with that for respiratory period obtained from the above of mammalian “mammalian design.” Dimensional constants, define
studies on individual animals may then be compared with predicted figures at a given weight, with the goal of demonstrating physiological specialization. The allometric coefficients and confidence limits of Table 1 can easily be further tested since they predict an unlimited number of specific values for respiratory variables. Interesting results would probably be obtained in studies of athletic versus pastoral mammals, cetaceans, high-altitude dwellers, and also in animals of more extreme weights, such as the mouse, horse, and possibly elephant or whale.

REFERENCES


Leong, K. J., G. F. Dowd, and H. N. MacFARLAND. A new...


