References and Notes

1. M. Talbot, *Amer. Midland Naturalist* **34**, 504 (1945); *Ecology* **44**, 549 (1963); P. B. Kannowski, *Symp. Genet. Biol. Italica* **12**, 74 (1963).
2. M. Talbot, *Psyche* **63**, 134 (1956); *Animal Behav.* **12**, 154 (1964); P. B. Kannowski, *Insectes Sociaux* **6**, 115 (1959).
3. E. S. McCluskey, *Science* **128**, 536, (1958).
4. ———, *Physiol. Zool.* **36**, 273 (1963).
5. The *Solenopsis* were obtained from E. O. Wilson's laboratory colonies. The *Camponotus*, collected from a colony near Yucaipa, Calif., were determined by W. L. Brown, Jr.
6. E. S. McCluskey, in preparation.
7. *Cold Spring Harbor Symp. Quant. Biol.* **25** (1960).
8. F. Reichle, *Z. Vergleich Physiol.* **30**, 227 (1943); J. Dobrzański, *Folia Biol.* **4**, 385 (1956) (in Polish, with Russian and English summaries; French translation kindly supplied by author).
9. W. Grabensberger, *Z. Vergleich. Physiol.* **20**, 1 (1963).
10. O. Wahl, *ibid.* **16**, 529 (1932).
11. E. S. McCluskey, thesis, Stanford Univ., 1959 (University Microfilms, Ann Arbor, Mich.).
12. J. H. Eads and E. O. Wilson, special report to Alabama Dept. Conserv., 1949; N. Kusnezov, *Acta Zool. Lilloana* **18**, 385 (1962).
13. S. H. Skaife, *The Study of Ants* (Longmans, Green, London, 1961).
14. M. S. Blum, letter, 1965.
15. C. S. Pittendrigh, *Harvey Lectures* **56**, 93 (1961).

16. Supported by NSF postdoctoral fellowship 49101. It was a privilege to work in the Biological Laboratories; I especially thank E. O. Wilson.

* Present address: Department of Physiology and Biophysics, Loma Linda University, Loma Linda, Calif. 92354.

3 August 1965

Organ Weights in Primates and Other Mammals

Abstract. *In mammals the weight of the heart, kidney, lungs, and other organs can be related to total body weight through power laws (allometry). Weights of primate organs are analyzed by this technique. Allometric coefficients and size-independent organ-weight or body-form ratios may be used to compare primates, including humans, and other mammals.*

About 1895–1900 it was observed that the relative brain size of anthropoids was best assessed by use of parameters obtained from a log-log plot of brain weight against body weight. This analytical technique subsequently came to be known as "allometry," and was much advanced by a book by Julian Huxley (*1*). Huxley showed that the plotting of many gross body measurements against body weight or a reference body length yields straight lines on log-log paper. A massive collection of allometric data on organ weights and body-size parameters was provided by Brody (*2*). Subsequently it was demonstrated (*3, 4*) that the allometric technique could also be applied to body minerals and fluids, many physiological parameters, muscle masses, a variety of skeletal measurements, and other parameters.

This report presents allometric data (Table 1) on the weight of the principal organs (heart, lungs, liver, kidneys, adrenals, thyroid, pituitary, spleen, pancreas, and brain) of primates and "mammals" (which here designates mammals other than primates). Statistical analysis reveals that the allometric prediction equations are reliable and that the coefficients in these equations appear to be statistically indistinguishable for the primate and mammalian groups, except in the case of the brain. It is also pointed out that one may form size-independent ratios of organ weights which constitute dimensionless organismal "shape factors."

The weight data for mammalian organs were obtained from Brody (*2*, chap. 17). He includes all necessary statistical measures except for total numbers of animals, but these were large, as is seen from the graphs of his regression lines. Brody does not give satisfactory prediction equations for the pituitary, pancreas, or spleen of mammals. Data on organ weights, from an extensive collection of such data by Crile and Quiring (*5*), were used to obtain the parameters shown for the spleen and pituitary in mammals in Table 1; there are not enough published data on the pancreas to enable allometric coefficients to be obtained for mammals. The mammalian prediction equations are known to be valid in the size range from mice (25 g) to steers (500 to 1000 kg), and may even apply to elephants and whales.

Data on weights of primate organs were obtained from published reports of Hrdlicka (*6*), Crile and Quiring (*5*), Kennard and Willner (*7*), and Herrmann *et al.* (*8*). New data collected at the Oregon Regional Primate Research Center during the last 4 years [Knezevic (*9*), Malinow (*10*)] were also included. There were 321 data points found for primate hearts, with lesser numbers for other organs. As shown in Figs. 1 and 2, the size range of primates covered is from tree shrews (less than 10 g) to humans (70 kg), with limited data on the gorilla (over 100 kg). The points in Figs. 1 and 2 identify authors of data, not kinds of animals, and include a considerable range of body sizes for each kind of primate named, for example, weights of 2 to 10 kg for macaque monkeys. However, most of the primate data are from animals which are of at least "young adult" age. The prediction curves are for organ weights in mature animals of various sizes, and not for organ size during growth and development as such. Data on howler monkeys, collected by Malinow (*10*) at this Center, do include some for fairly young animals, but they fit the general prediction formulas in a satisfactory manner.

The organ weights were analyzed against body weight by a regression analysis, with a SDS-920 computer (*11*). Statistical formulas for fitting the allometric equations $y = a\ x^b$ are provided by Brody (*2*, pp. 398–401 and other pages). In this report, organ weight (y) is given uniformly in grams; body weight (x), in kilograms. Allometric parameters were obtained by a least-squares fit after conversion to $\log_{10}$ values. The a parameter is the value of the ordinate at a body weight of 1 kg. In view of the log-log transformation, the most useful measure of precision for the a value is its standard error, given as a percentage of the mean value. The parameter $S_{a\%}$ is this statistic for a, and represents the 67-percent confidence limit; 95-percent confidence limits are given by twice $S_{a\%}$. The log-log plot slope value is given directly as b; S_b is the standard error of the slope in absolute slope units.

An indication of the validity of the entire plot is given by the value of the correlation coefficient r and the standard deviation of data points from the prediction line, as indicated by the standard error of the estimate (S) in Table 1. For all cases shown in this table, correlations were significant at the .01 level of confidence. There has been considerable discussion of the best techniques for fitting allometric data (*12*), but the cited statistical parameters appear to be adequate.

Table 1 and Figs. 1 and 2 show that the mammalian and primate prediction equations are almost identical, with the major exception of the brain. In the case of the heart, lungs, kidneys, pituitary, and spleen the 1-kg intercept (a) and slope (b) parameters lie within one standard error of each other, while for the liver, adrenals, and thyroid the a and b values are at worst within two standard errors of each other.

This conclusion is confirmed by Figs. 1 and 2, which compare Brody's previously published lines for mam-

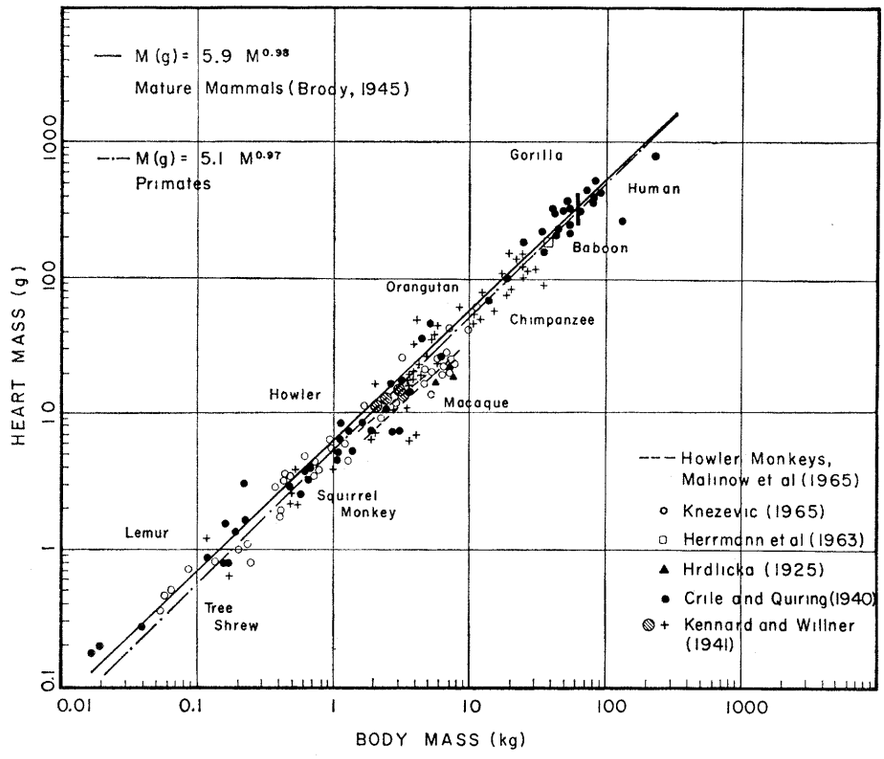

Fig. 1. Heart weights in mammals and primates. The solid line is based on Brody's (*2*) prediction formula for mammals in the mouse to steer-or-larger range. The dashed line is a statistically fitted plot based on 321 primates ranging in weight from about 10 g to 100 kg. All of the authors cited studied a variety of animals, as shown by approximate adult weights. The mammalian and primate allometric lines are statistically indistinguishable in this study. Independently computed lines for growing howler monkeys (Malinow, *10*) are also given.

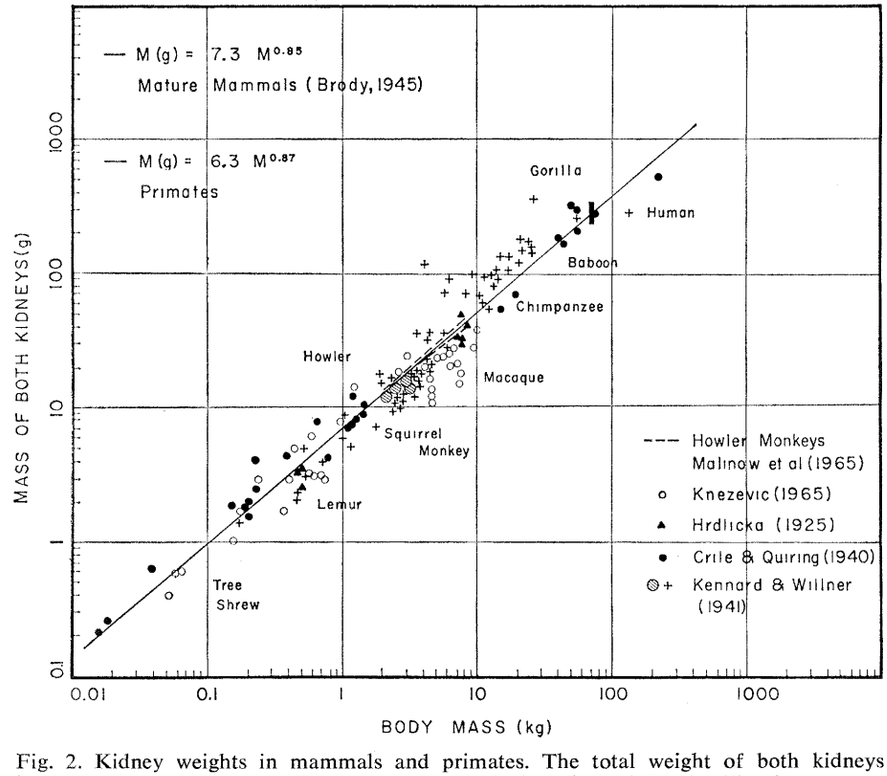

Fig. 2. Kidney weights in mammals and primates. The total weight of both kidneys is shown on the ordinate. The allometric prediction line of Brody (*2*), shown as a solid line, is found to be nearly identical with a new line for primates, based on 268 animals. Prediction lines for growing howler monkeys. (Malinow, *10*) are found to fit the plot for mature animals with unexpected accuracy.

mals with the newly computed primate prediction lines. In the case of the kidney the lines were too close together to even allow separate plotting, while for the heart they differ by only about 13 percent at the comparison point for 1 kg. Figures 1 and 2 also include prediction lines for howler monkeys, recently obtained by Malinow (*10*) as the result of studies on 316 animals with a weight range of 1 to 10 kg. Malinow's findings include fairly young animals, but no infants; his prediction lines agree with the formulas for weights of organs of mature animals.

From Table 1 it is clear that the standard error is 25 to 90 percent for most mammalian and primate organs. This represents a relatively low level of accuracy for prediction of organ weights in a particular animal of known weight, but nevertheless the linearization of data over more than four orders of magnitude of body weight is impressive. The same sort of general result has been obtained in almost all published allometric studies, which are best suited for demonstrating "size effects" and body form relationships. More refined prediction equations, including effects of age, sex, body fat content, and so forth, must be used to obtain satisfactory estimates in, for example, humans suspected of having organs enlarged or shrunken by disease. Problems of this nature are discussed elsewhere (*13*) in more detail.

The brain differs from all other organs in Table 1 in that its 1-kg intercept value (*a*) clearly distinguishes mammals and primates, and also the major groups of primates. The slope of the allometric line is quite constant in the range of 0.64 to 0.75 for all mature mammals, including primates; during growth and development, plots of brain weight may give *b* values of 0.25 to 0.50. Jerison (*14, 15*), Stephan and Andy (*16*), Scholl (*12*), and others have analyzed relative brain size in primates and shown that *a* coefficients from allometric plots are useful numerical criteria of "cephalization." Moreover, one may compare development of specific parts of the brain, for example, cortex, olfactory bulb, midbrain, and so forth, by the allometric technique, to give more detailed insight into relative enlargement of the brain during phylogenesis (*16*).

It could hardly be expected a priori that organ weights would be so well linearized by log-log plots, or that the

characteristic parameters for mammals and primates would be identical within presently available statistical limits. These observations suggest that all mammals have in common a basic kind of "physiological design."

In a series of prior reports (*3, 4, 17*) I have pointed out that engineering dimensional analysis and modeling theory can be used to compare mammals as "physical systems." Physical similarity of this type is defined specifically by invariance of sets of dimensionless numbers or "criteria of similarity." Genetic, behavioral, biochemical, and other types of functional similarity are not covered by this definition. Dimensionless similarity criteria may be obtained by forming quotients of power-law prediction equations, as shown by the following examples based on the primate data:

$$\frac{\text{heart weight (g)}}{\text{body weight (g)}} = \frac{5.2\ M^{0.98}}{1000\ M^{1.0}} = 0.0052\ M^{0.02}$$

$$\frac{\text{heart weight (g)}}{\text{lung weight (g)}} = \frac{5.2\ M^{0.98}}{11.3\ M^{0.99}} = 0.46\ M^{-0.01}$$

$$\frac{\text{liver weight (g)}}{\text{kidney weight (g)}} = \frac{33.3\ M^{0.87}}{7.3\ M^{0.85}} = 4.5\ M^{0.02}$$

Since any number to the zero power is equal to unity, the small and statistically insignificant residual mass exponents (0.02, −0.01, 0.2) indicate that body weight has little or no effect, as such, on the indicated dimensionless "body form" ratios.

The same technique can be applied to allometric equations predicting physiological functions (*17*). From this, one obtains simple or complex physiological dimensionless similarity criteria which define the extent of "physical similarity" between two groups of animals that occur in a range of adult sizes. The invariance of dimensionless numbers is used to define "physical models" in the engineering sense. Artificial organs are found to be partial physical models of the natural ones (*4, 13*) to the extent that they are governed by the same physical similarity criteria. However, such model organs do not allow quantitative prediction about organs *in situ* because the latter are also governed by many dimensionless and dimensional constants not represented in the artificial systems.

Table 1. A comparison of organ weights in primates and mammals. Organ weight (grams) = $a\ M^b$ with body mass M in kilograms; $S_{a\%}$, standard error of the a parameter shown as mean of plus and minus deviations; S_b, standard error (absolute value) of the slope parameter b; N, number of animals; r, regression coefficient; S, standard error of the estimate.

Organ and animal	a	$S_{a\%}$	b	S_b	N	r	S
Heart							
Mammals*	5.8	41%	0.98	0.01	>100	0.99	
Primates	5.2	28%	.97	.02	321	.99	0.11
Lungs							
Mammals*	11.3	50%	0.99	0.01	>100	0.96	
Primates	9.7	45%	.94	.04	268	.95	0.16
Liver							
Mammals*	33.3	36%	0.87	0.01	>100	0.99	
Primates	32.2	28%	.93	.02	293	.98	0.11
Kidneys							
Mammals*	7.3	38%	0.85	0.01	>100	0.99	
Primates	6.3	45%	.87	.04	268	.95	0.16
Adrenals							
Mammals*	0.27	65%	0.80	0.02	>100	0.97	
Primates	.53	69%	.70	.05	304	.88	0.23
Thyroid							
Mammals*	0.13	75%	0.92	0.02	>100	0.97	
Primates	.15	74%	1.12	.06	225	.94	0.24
Pituitary							
Mammals†	0.03	25%	0.56	0.02	60	0.99	0.10
Primates	.03	71%	.68	.12	147	.72	.23
Spleen							
Mammals†	2.5	90%	1.02	0.05	75	0.98	0.28
Primates	1.5	72%	0.85	.10	44	.93	.23
Pancreas							
Primates	2.0	43%	0.91	0.06	201	0.92	0.16
Brain							
Mammals*	10	51%	0.70	0.01	>100	0.97	
Mammals‡	9.3	>50%	.73		108	.98	
Monkeys‡	20 to 30	22%	.66		50	> .9	
Great apes‡	30 to 40	25%	.66		35	> .9	
Humans‡	80 to 90	18%	.66		50	> .9	

* Mammalian data from Brody (*2*). † Newly computed mammalian data, based on values in Brody (*2*) and Quiring and Crile (*5*). ‡ Brain weight coefficients from Jerison (*14*) and other sources.

Anthropometry is based on dimensionless ratios of body lengths applied to the comparison of body shape in related anthropoids. More than 40 specific form ratios of this type have been defined by anthropologists with the goal of comparing primates and human races.

There is, in general, no well-defined technique for singling out specific ratios as being "more fundamental" than others, except on the basis of general impressions of experienced taxonomists. The same is true of the organ weight and physiological dimensionless ratios. For example, it is known that heart weights are relatively greater in greyhounds and race horses, but a change in this ratio cannot be said to be taxonomically more or less important than alterations in skeletal ratios observed among strains of dogs or horses. Relative heart weights appear to provide little insight into phylogeny.

Size-independent dimensional constants may also be deduced by the allometric cancellation method. For example, log-log plotting of blood volume in mammals (*17*) yields the highly significant prediction formula: Volume of blood (cm^3) = $70M^{1.0}$. Dividing by body weight gives the size-independent dimensional constant 70 ml of blood per kilogram of body weight. Many other constants of this type are reported elsewhere (*13*).

The primates represent an especially interesting group from the viewpoint of physical-similarity analysis. Studies are under way on a variety of form measurements and physiological parameters in primates and have already yielded numerical parameters which are useful for empirical comparisons of body form and physiological performance in primates. It is interesting to discover that engineering modeling theory may be applied in a straightforward manner for comparisons of animals from the standpoint of physical system design and comparative performance. An approach of this type was clearly anticipated by Thompson (*20*), who suggested that some aspects of biological form should be interpreted from a purely physical viewpoint.

WALTER R. STAHL
Department of Biomathematics and Automatic Data Processing, Oregon Regional Primate Research Center, Beaverton, Oregon

References and Notes

1. J. S. Huxley, *Problems of Relative Growth* (Methuen, London, 1932).
2. S. Brody, *Bioenergetics and Growth* (Reinhold, New York, 1945).
3. W. R. Stahl, *Science* **137**, 205 (1962).
4. ———, *Advan. Biol. Med. Phys.* **9**, 356 (1963).
5. G. Crile and D. P. Quiring, *Growth* **4**, 291 (1940).
6. A. Hrdlicka, *Am. J. Phys. Anthropol.* **8**, 201 (1925).
7. M. A. Kennard and M. D. Willner, *Endocrinology* **28**, 955, 967, 977 (1941).
8. G. H. Herrmann *et al.*, *Proceedings of the First International Symposium on the Baboon, Nov. 1963* (Southwest Foundation for Research Education, San Antonio, Texas).
9. A. Knezevic, "Autopsy findings obtained at the Oregon Regional Primate Research Center." Supplied to author by courtesy of Drs. A. Knezevic and W. McNulty.
10. M. R. Malinow, *Biology of the Howler Monkey*, in press.
11. The assistance of Dennis Lindgren, Robert W. Coffin, and L. B. Lusted of the Department of Biomathematics and Automatic Data Processing at the Oregon Regional Primate Center, is gratefully acknowledged.
12. D. Sholl, *Proc. Roy. Soc. London, Ser. B.* **135**, 243 (1948).
13. W. R. Stahl, *Physiological Modeling and Performance Analysis*, in preparation.
14. H. J. Jerison, *Science* **121**, 447 (1955).
15. ———, *ibid.* **133**, 1012 (1961).
16. H. Stephan and O. J. Andy, *Am. Zoologist* **4**, 59 (1964).
17. W. R. Stahl, *Proc. 17th Conf. on Engineering in Med. and Biol., Cleveland, Nov. 1964* **6**, 60 (1964); *Proc. 18th Conf. on Engineering in Med. and Biol., Philadelphia, Nov. 1965*, in press.
18. H. Lumer and A. H. Schultz, *Human Biol.* **13**, 283 (1941).
19. E. H. Ashton and S. Zuckerman, *Am. J. Phys. Anthropol.* **9**, 283 (1951).
20. D'A. W. Thompson, *On Growth and Form* (Cambridge Univ. Press, New York, ed. 2, 1959), vol. 1.

21. Publication No. 83 of the Oregon Regional Primate Research Center. Supported in part by NIH grant FR 001634 and PHS grant GM 13605-01.

26 August 1965

Phenylketonuria: Limit in Capacity of Pre-Weanling Rats To Oxidize β-Phenyllactate and Other α-Hydroxy Acids

Abstract. *In comparison with mature animals, pre-weanling rats have markedly higher and longer lasting serum levels of β-phenyllactate following the intraperitoneal injection of a moderate dose. A corresponding age-dependent difference in the rate of oxidation of β-phenyllactate and other α-hydroxy acids was observed in experiments with homogenates and supernatant fractions of rat kidney.*

The possibility that the oxidation of some long-chain α-hydroxy acids might be significantly limited during an early postnatal stage was noted in the course of studies with phenylalanine-loaded rats (*1*). Pre-weanling rats receiving high doses of L-phenylalanine by repeated intraperitoneal injection deaminated the amino acid and reduced the resulting phenylpyruvate efficiently, but accumulated considerably more phenyllactate than more mature animals did under comparable conditions. The findings suggested the development or augmentation within a brief interval of a key system affecting the relative concentrations and, possibly, the absolute amounts of phenylpyruvate and phenyllactate in the body fluids. The large increase in the ratio of phenylpyruvate to phenyllactate in the urine which occurred between the 18th and 25th days of age, with concomitant reduction of phenyllactate concentrations in serum and brain tissue, suggested an increased capability in conversion of the hydroxy to the keto form. Since, in the case of phenyllactate, this oxidative step intervenes between a metabolic dead-end and access to a main artery of aromatic metabolism (tyrosine formation), the activity of the system would concern phenylalanine metabolism under certain conditions and should be rate-limiting in the metabolism of administered phenyllactate.

Measurements of serum phenyllactate concentrations following intraperitoneal administration of a single small dose (100 mg/kg) of the hydroxy acid to rats at varying developmental stages are shown in Fig. 1. These results clearly demonstrate the comparative inability of the infant rats to deal effectively with injected phenyllactate. For periods of more than 3 hours, relatively high concentrations of the hydroxy acid persisted in the blood of animals less than 18 days of age (30 g with this colony), whereas much lower and rapidly declining levels were observed with older animals treated similarly.

Kidney has been the tissue of choice for studies on the oxidation of α-hydroxy acids. The relative rates of L-phenyllactate oxidation by homogenates and 30,000*g* supernatant fractions of the kidneys from rats of different ages are shown in Fig. 2. At least a ninefold increase was apparent in a comparison of the activities of equivalent fresh weights of tissue from rats progressing from infancy to an adult stage (200 g). Based on the yield of phenylpyruvate per gram of tissue during the 30-minute incubation period, activity increased at an apparently linear rate from an observed low value of 1 μmole in the case of 2- to 3-day-old rats to nearly 10 μmole with fully matured animals. Kidney weight also increased linearly during the same period, but less than a twofold increase in D-amino acid oxidase activity was noted in a similar assay system with D-phenylalanine as substrate.

With the α-hydroxy derivatives of valeric, caproic, and caprylic acids and with *p*-hydroxyphenyllactate, however, age-dependent increases similar in magnitude to that encountered with phenyllactate were indicated (Table 1). A number of aliphatic α-hydroxy acids, indole lactate, indole glycollate, and α-phenyllactate inhibited the con-

Table 1. Oxidation of higher α-hydroxy acids by kidney extracts prepared from rats of differing degrees of maturity. Each value represents the activity during 30 minutes of a 30,000*g* supernatant fraction equivalent to 0.3 g (fresh weight) of tissue. The incubation mixtures consisted of 0.5 ml of buffered extract and 10 μmole of a DL-α-hydroxy acid or approximately 7.5 μmole of an α-keto acid in a total volume of 1.5 ml. Incubation conditions were the same as those described in the legend of Fig. 2. α-Keto acid controls were deproteinized at zero time. The method of Penrose and Quastel (*19*) was used to determine the concentration of α-keto acid.

Addition	α-Keto acid (μmole)			
	26 g*	73 g*	100 g*	270 g*
	Increase in α-keto acid			
DL-α-Hydroxyvalerate	0.3	3.8	4.1	5.0
DL-α-Hydroxycaproate	.6	2.9	3.0	4.6
DL-α-Hydroxycaprylate	< .3	2.0	2.1	4.1
DL-β-Phenyllactate	< .3	1.3	1.5	2.9
DL-*p*-Hydroxy-β-phenyllactate	< .3	0.7	1.0	1.7
	Decrease in α-keto acid			
α-Ketovalerate	0.1	0.2	0.2	0.2
α-Ketocaproate	.3	.6	.4	.4
Phenylpyruvate	.7	.4	.3	.7
p-Hydroxyphenylpyruvate	.7	.8	.7	.7

* Average weight of rat.