

THE RELATIONSHIP BETWEEN MAMMALIAN FOETAL WEIGHT AND CONCEPTION AGE

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(Received 18 November 1950)

Sheep foetal weight and length data have been collected for the purpose of checking foetal age and in the course of this work it has been found that the cube root of the foetal weight gave a linear plot with age from the 50th day of pregnancy to full term. The purpose of this paper is to describe this result and to indicate how the cube root relationship may be extended to other mammalian data, and to discuss its significance in comparative foetal physiology.

Early attempts to find empirical formulae relating foetal weights to age from conception have been extensively reviewed by Needham (1931). The majority of these involved a linear relationship between weight and a power (approximately the third power) of the time or, alternatively, a relation between time and a cube or higher root of the foetal weight.

Greater precision was brought to such formulae by McDowell, Allen & McDowell (1927) who introduced the concept of embryo age and obtained a formula, essentially of the power type, relating log weight and log embryo age. The embryo age was arbitrarily determined to commence with the appearance of the primitive streak (7.2 days for mouse embryos, 12 days for guinea-pigs), and the powers obtained varied from 3.65 to 3.99 for the mouse and guinea-pig respectively.

The power obtained in this way is very sensitive to small changes in the arbitrarily fixed zero embryo age which has no sound physiological basis.

If a steady state of growth exists during foetal development one would expect it to be most free from complications when the foetus has the environmental stability such as provided by an established placental circulation. It would be an advantage therefore if weight and age data for the last half or two-thirds of pregnancy could be represented without using the arbitrary expedients necessary with logarithms.

This problem faced us in our endeavour to obtain a representation of collected data of weights and lengths of foetuses from Welsh ewes, which could be used for checking foetal ages.

METHOD

In the course of experiments on pregnant Welsh ewes over four breeding seasons, foetal weight and length measurements have been taken as a routine. The length measurements made were two in number—both from the frontal boss to the root of the tail (boss to rump, B-R). The first was a direct B-R length measured with a straight edge on the body; the second, a circumferential B-R length measured with a tape following the contour of the dorsal midline. In both cases the dead foetus was laid out straight lying on its side on a flat surface and was unstretched. The mean of these two lengths (L) gives a reasonably linear plot against foetal age (Fig. 1) similar to the plot of crown-rump length and age given by Barcroft & Kennedy (1939) and by Barcroft (1946). The results were analysed statistically and the regression line obtained from the data of 55 singletons was $L=0.45(t-34)$ where t represents the conception age in days and L the mean B-R length in cm. The 95% confidence limits are indicated by the dotted lines in Fig. 1.

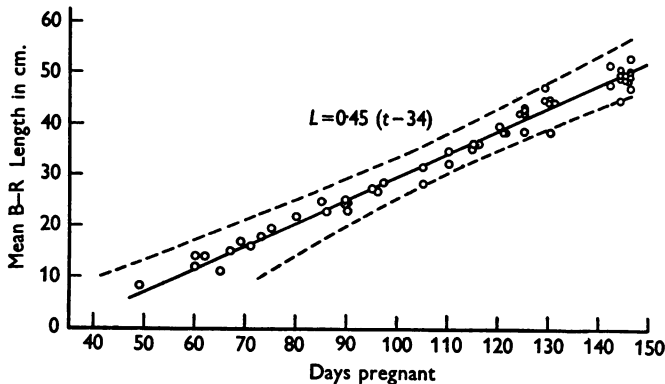


Fig. 1. Plot of mean B-R length for foetal sheep against conception age. Regression line $L=0.45(t-34)$, where t is conception age in days. 95% confidence limits represented by dotted lines.

The weight measurements were the weight of the dead foetus alone (i.e. without placenta or fluids). Weights were expressed in grams. In the ordinary way, weight data could not be analysed statistically and a plot of log weight was found to be concave to the time axis. But if, as shown in Fig. 1, the B-R length increases linearly with age, one would expect, on a principle of similitude, that the volume or weight would tend to increase as the cube of the age or the cube root of the volume or weight as the age. Since the line relating B-R length and age intercepts the time axis at 34 days and not at zero it was decided to plot the cube root of the weight against foetal age.

RESULTS

Foetal weight and age data

The weight data from 55 singleton sheep fetuses are represented in Fig. 2 where the cube root of the weight has been plotted against conception age. Expressed in this way a reasonably linear plot was obtained which could be treated statistically, the regression of $W^{\frac{1}{3}}$ on age giving the formula

$$W^{\frac{1}{3}} = 0.147(t - 37), \quad (1)$$

while the regression of age on $W^{\frac{1}{3}}$ gave the formula

$$W^{\frac{1}{3}} = 0.149(t - 38.6). \quad (1a)$$

The confidence limits are again indicated by the dotted lines. (Theoretically, estimations of age ought to be based on the regression of age on cube root of weight, but for practical purposes the two regression lines show only trivial differences.)

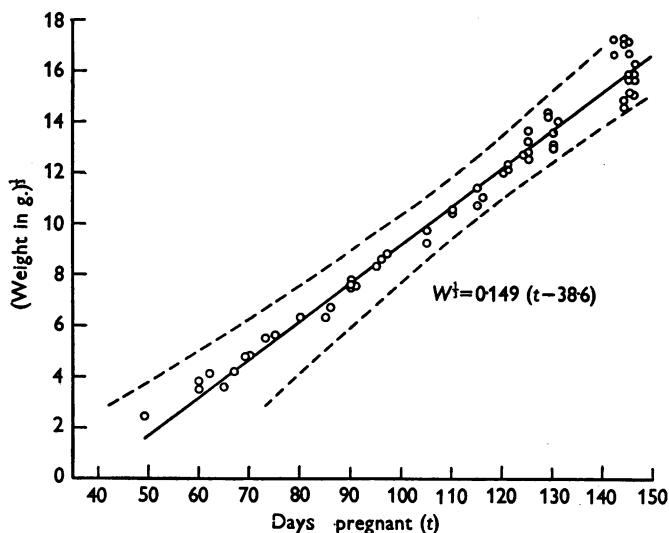


Fig. 2. Plot of cube root of weight of foetal sheep against conception age. Continuous line drawn to equation $W^{\frac{1}{3}} = 0.149(t - 38.6)$; 95% confidence limits indicated by dotted lines.

This representation of weight coupled with the plot of B-R lengths proved satisfactory in checking the age of sheep foetuses where 'tupping' dates were in doubt and has been reported elsewhere (Huggett & Widdas, 1950). It was, however, decided to investigate whether this method of representing foetal weights could be applied to other mammals. For this purpose foetal weight and age data published by various authors have been used. In these cases statistical analysis was not used to obtain the equation of the line, since most of the points represent means, but lines have been fitted by inspection and are to this extent therefore tentative.

The data first available were those due to Hammond (1914) on foetal rabbits quoted in Barcroft's *Researches on Prenatal Life* (1946), and are represented in Fig. 3. Apart from the first two points which represent foetuses of 10 and 70 mg. respectively, the linearity of $W^{\frac{1}{3}}$ against age is reasonable.

The weight data for the embryo mouse obtained by McDowell *et al.* (1927) represented in the same way are shown in Fig. 4. The results fall satisfactorily about a line having the formula

$$W^{\frac{1}{3}} = 0.102(t - 8) \quad (2)$$

and the intercept at 8 days may be compared with 7.2 days arbitrarily deducted by the above authors in estimating embryo age.

A similar representation of Draper's smoothed data (1920) for the guinea-pig foetus is shown in Fig. 5. These results fall about a line having the formula

$$W^{\frac{1}{3}} = 0.09(t - 16) \tag{3}$$

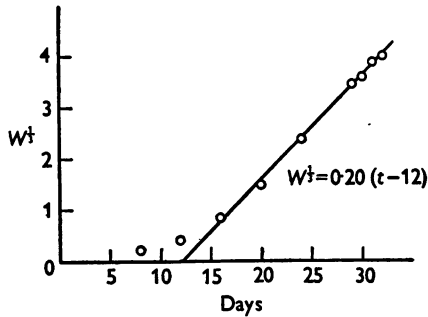


Fig. 3. Plot of cube root of weight against conception age for foetal rabbit. Weight data from Hammond (1914).

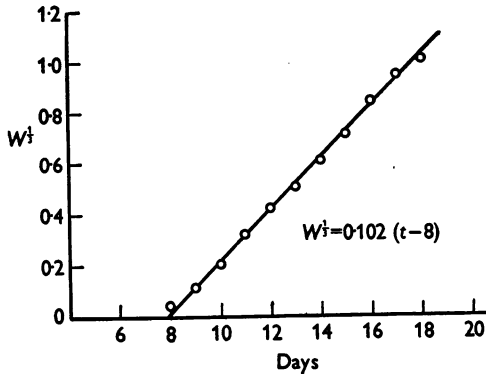


Fig. 4. Plot of cube weight against conception age for embryo mouse. Continuous line drawn to equation $W^{\frac{1}{3}} = 0.102(t - 8)$. Weight data from McDowell *et al.* (1927).

which is as good a fit to the data from 20 days to full term as can be expected from any simple formula.

In Fig. 6 Friedenthal's (1914) data for the human foetus are represented in this manner and although the fit here is less satisfactory than in earlier examples it is unlikely that conditions could be so uniform as is possible in animal experiments. Data for the rat, pig and cow have been treated in similar fashion.

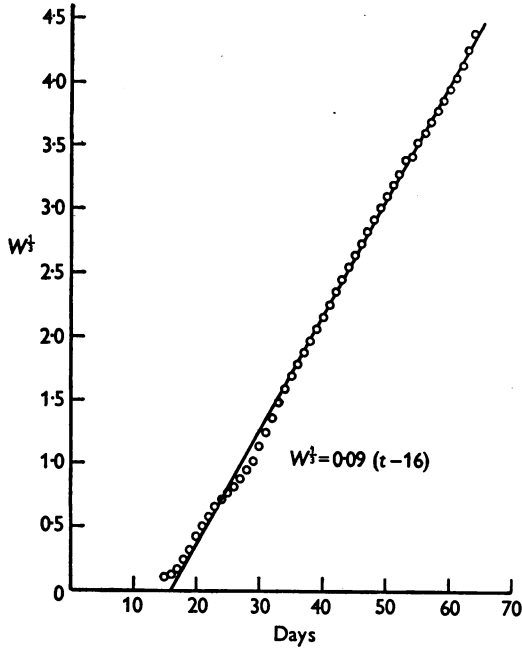


Fig. 5. Plot of cube root of weight against conception age for foetal guinea-pig. Continuous line drawn to equation $W^{1/3} = 0.09(t - 16)$. Weight data from Draper (1920).

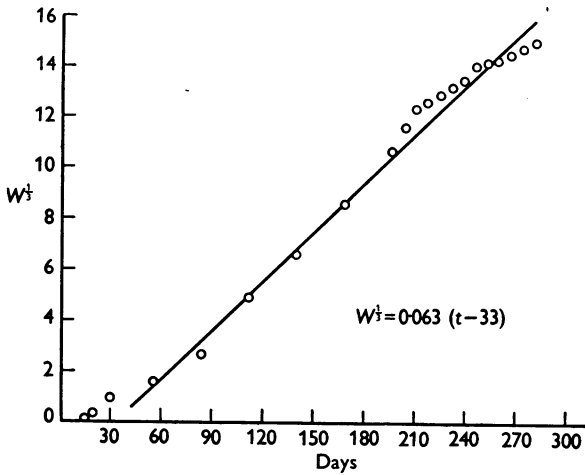


Fig. 6. Plot of cube root of weight against conception age for human embryo. Continuous line drawn to equation $W^{1/3} = 0.063(t - 33)$. Weight data from Friedenthal (1914).

Use of birth and weight gestation times

Data of intrauterine foetal weights and ages are available for only a limited number of mammals and thereby limit the scope of comparative study, but if it can be accepted that foetal development during a substantial part of pregnancy up to full term can be adequately expressed by a general formula of the form

$$W^{\frac{1}{3}} = a(t - t_0), \tag{4}$$

then it is possible to use birth weight and gestation time data and so extend the field of comparison.

Since $W \propto \text{volume} \propto L^3$ from equation (4)

$$a = \frac{W^{\frac{1}{3}}}{t - t_0} \propto \frac{[L]}{[T]},$$

that is, dimensionally, a may be taken as a velocity.

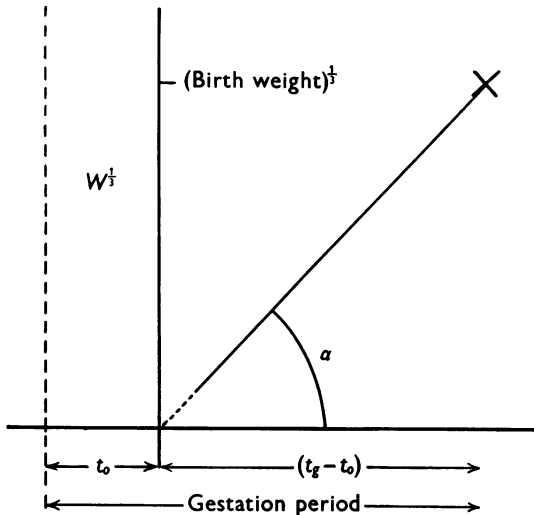


Fig. 7. Illustration of way in which birth weight and gestation time data can be used to determine a , the specific foetal growth constant. For details see text.

For the present purpose a may be termed the *Specific Foetal Growth Velocity* and is the slope of the line relating $W^{\frac{1}{3}}$ and age (t) as indicated in Fig. 7.

It is peculiar to the mammal concerned and is most suitable for comparing rates of foetal development in different mammals.

The term t_0 is the intercept where the linear part of the plot, if produced backwards, cuts the time axis. It has no clear biological significance, in foetal development, but if the numerical value of t_0 can be estimated from analogy with other mammals for which foetal weight and age data are available, then one known weight (W) and time from conception (t) would be sufficient to determine the value of a for the mammal concerned.

TABLE 1. Formulae from published intrauterine weights and ages:

$W\frac{1}{3}=0.102(t-8)$	Mouse
$W\frac{1}{3}=0.17(t-11)$	Rat
$W\frac{1}{3}=0.20(t-12.5)$	Rabbit
$W\frac{1}{3}=0.09(t-16)$	Guinea-pig
$W\frac{1}{3}=0.147(t-37)$	Sheep
$W\frac{1}{3}=0.145(t-50)$	Cow
$W\frac{1}{3}=0.063(t-33)$	Human

General formula $W\frac{1}{3}=a(t-t_0)$

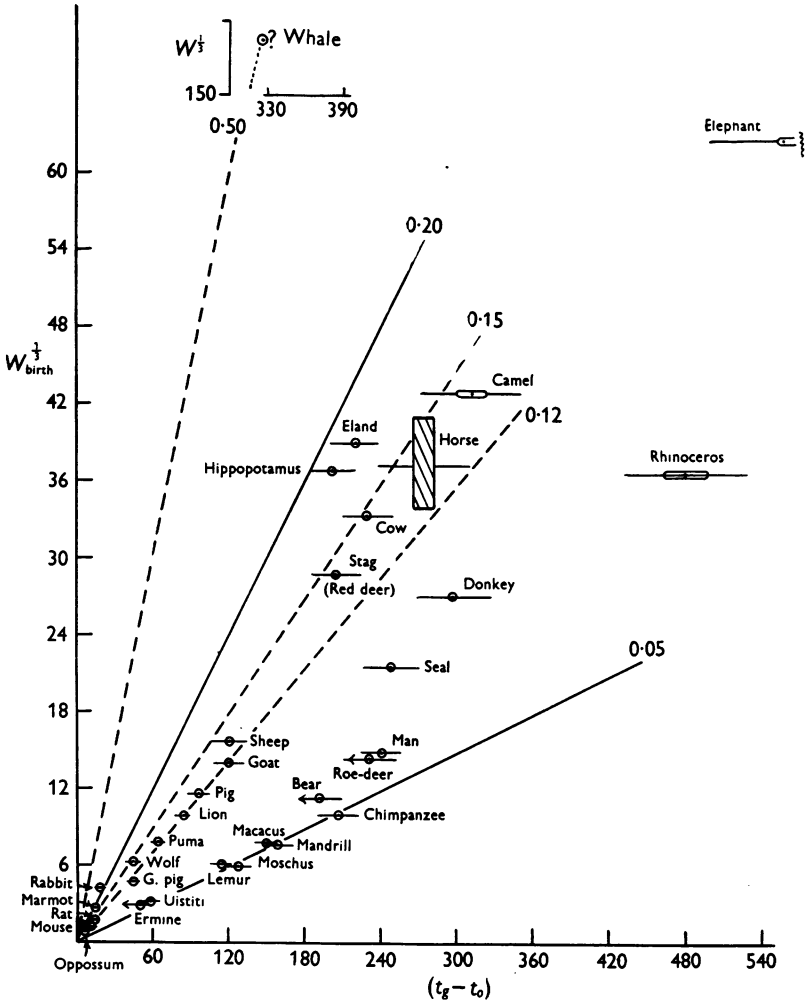


Fig. 8. Plot of cube root of birth weight against gestation time less the estimate of t_0 . Continuous lines through the origin indicate the range of values of a . Chart compiled from data due to Przibrám (1927).

The values used can be the birth weight and the total gestation time and in consequence, if the cube root of the birth weight is plotted against gestation

time less the estimate of t_0 , the line from the point to the origin will give the slope a .

The estimate of t_0 from the existing data (Table 1) is based on the observation that t_0 increases as gestation times lengthen but forms a decreasing fraction of the total gestation time.

In spite of the approximations which must necessarily be used, the procedure shows certain remarkable features which are illustrated in Fig. 8, compiled from Przibram's data (1927). In analysing these data the following arbitrary estimates of t_0 have been used; for gestation times up to 50 days $t_0 \approx 0.4 \times$ (gestation time), from 50–100 days $t_0 \approx 0.3 \times$ (gestation time), from 100–400 days $t_0 \approx 0.2 \times$ (gestation time), over 400 days, $t_0 \approx 0.1 \times$ (gestation time).

These approximations may introduce an error in the specific growth rate of the order of 15% in the slopes for animals of short gestation period. The errors from this cause for mammals with gestation periods over 50 days is unlikely to exceed 10% unless some factor such as delayed implantation is also present. These errors are indicated by the horizontal lines through the points in Fig. 8.

The first feature of note is that there is a lower range of the specific foetal growth velocity where $a \approx 0.05$, in which are found the Primates, including uistiti, lemur, macacus, mandrill, chimpanzee and man. The only non-Primates in this region are the ermine, bear, roedeer and moschus, all except the last quoted by Asdell (1946) to be animals in which delayed implantation occurs, a circumstance which has not been allowed for in the estimation of the constant t_0 . An increased value of t_0 would reduce $(t - t_0)$ and displace the points representing these mammals to the left as indicated by the arrows.

The highest value of a (0.20), greater than a for Primates by a factor of 4, is represented by the marmot, rabbit, hippopotamus and eland, but the majority of mammals quoted fall on an intermediate range in which $a \approx 0.12 - 0.15$ cm./day.

DISCUSSION

The ideas of a one-third power relationship between foetal weight and conception age was first advanced by Roberts (1906). Later Balthazard & Dervieux (1921) put forward the formula $T = 19.4 \times \sqrt[3]{W}$ for the human embryo and Schmalhausen (1927) reported that for the chick embryo $\sqrt[3]{W} \propto T$. Murray (1926), also using the chick embryo, found that his results were well represented by the relation $\sqrt[3.6]{W} \propto T$.

All these formulae were endeavours to relate weight and time measured from date of conception without making any allowance such as advocated by McDowell *et al.* (1927). The results in Figs. 2–6 show that the cube root relationship is not one which can be made to fit when age is measured from conception, but nevertheless, adequately expresses foetal development over a substantial period of pregnancy when expressed in terms of a general formula

such as (4) containing a constant term t_0 which must be deducted from the conception age.

This formula, which is simple and easy to work with in the laboratory for checking foetal ages, also provides a constant which is the specific foetal growth velocity and which can be used in comparing foetal development in different mammals. Previous authors have tended to regard the coefficient $\log \text{weight} / \log \text{time}$ as the growth velocity but without a dimensional justification.

The influence of the number of young on this growth velocity is less than might be expected. In the sheep, for instance, lengths and weights of twins up to 90 days do not differ significantly from singletons. Beyond 90 days the individual weight increase falls off relative to singletons but the slope of W^t plotted against time only decreases from 0.147 to 0.122 during this period. In the rat, analysis of weight data from 120 litters does not show any significant decrease in foetal weights with increasing litter size (Table 2). The growth velocity would therefore appear to be determined not so much by the parent's ability to nourish and maintain the growing foetus or foetuses, as by the foetuses themselves.

TABLE 2. Relation between average individual foetal weight (g.) and litter size

Foetal age days	Litter size											Mean foetal weights and number of foetuses
	1	2	3	4	5	6	7	8	9	10	11	
13	—	—	—	—	—	0.050	—	0.040	—	—	—	0.045 (14)
14	—	—	—	0.103	0.127	—	0.192	—	0.115	—	—	0.134 (26)
15	—	—	—	—	—	0.227	0.281	0.236	0.270	0.272	—	0.265 (93)
16	—	—	—	0.476	0.382	0.434	0.420	0.439	0.444	0.381	0.464	0.428 (287)
17	—	—	0.683	—	0.671	0.750	0.764	0.727	0.790	—	—	0.742 (140)
20	3.65	—	—	3.04	2.74	2.253	2.28	2.83	—	—	—	2.81 (43)
21	4.50	—	—	4.46	—	4.01	4.91	4.49	3.96	—	—	4.32 (70)

Note. Included in these figures are two litters, one of 13 foetuses 16 days old, average weight 0.410 g., and the other of 16 foetuses 21 days old and average foetal weight 4.52 g. The bracketed numerals in the last column are the total number of foetuses weighed to give the mean.

Comparisons of the specific growth velocities of different mammalian foetuses would appear to show considerable promise. Although for the present relying on birth weights and gestation times, the differences between the Primates and other mammals are much greater than could be accounted for by possible errors in the approximations used. The clear-cut grouping of Primates suggests a genetical influence on the different rates of foetal development.

It is interesting to note that among the mammals in the intermediate range of Fig. 8, the period of linear growth is determined by the size of the foetus at birth. Thus, as the birth weight of the young is increased the mammal does not grow its young quicker, along a steeper slope, but must grow its foetus for a longer time. This will offer an explanation of Rubner's finding in 1908 that in all species except man the birth weight is proportional to the gestation time. Mammals producing the largest foetuses, such as the elephant, are obliged on the same principle to extend their period of gestation into a second year.

As it is almost universal experience that breeding cycles are synchronized with seasonal variations, this fact might suggest that because of some fundamental rule of nature a 1-year growth period for the elephant was not possible, or, in other words, that the limits of natural variation in specific foetal growth velocity are more or less represented by the continuous lines in Fig. 8.

Although the continuous lines of Fig. 8 may represent the limits of natural variation for land mammals, the Cetacea, which are sometimes referred to as the most aberrant mammals, must be gross exceptions. The gestation period for Blue and Fin whales is generally held to be under 1 year and analysis of length data provided by the International Whaling Statistics, by methods such as those followed by D'Arcy Thompson (1942), leaves little room to doubt such estimates. During this period a whale foetus weighing 3-4 million grams is produced. Whaling Statistics do not supply data of foetal weights, but if these foetuses follow a cube-root relationship, then the growth velocity ($a \simeq 0.50$) must be at least $2\frac{1}{2}$ times greater than the highest rate found for all other mammals, and about 10 times greater than the rate for Primates. It would be interesting to see if these high rates are peculiar to the large whales or are the same in related species of smaller size.

Since the substances contributing to weight increases are mainly water and protein followed by salts and other materials making up the complete organism, the chief biological significance of the different foetal growth rates must be seen in the rate of deposition of organic material, chiefly protein. Clearly we are dealing with three main variations of a fundamental characteristic of mammals in which whole sequences of processes are geared, presumably genetically, at three different rates.

It is not practical from the data to hazard any biochemical or physiological reason why, during this period of pregnancy, growth should follow a cube-root law—nor is it possible from the data to assert that a simple one-third power relationship is more accurate than some decimal power less than one-third. The practical reasons for using the simple cube root are mathematical convenience in handling weight data for checking foetal ages and the production of simple formulae which yield a specific growth velocity which is dimensionally sound and of considerable value for comparative purposes.

No simple formula is entirely satisfactory during the early days of pregnancy. Clearly the environmental conditions at this time may be such as to convert oxygen or nutrition supplies, hormonal and enzyme balance or allied factors into rate-determining steps. Delayed implantation as exhibited by certain mammals is an extreme example.

Certain considerations apply equally to a simple cube-root relation and to a more general fractional power relation. For instance, if the relationship be expressed as

$$W^n = a(t - t_0), \quad (5)$$

and this expression is differentiated with respect to time, we obtain

$$\frac{dW}{dt} = \frac{a}{n} W^{1-n}, \quad (6)$$

which gives the instantaneous growth rate. Where n is one-third this is proportional to the two-third power of the weight or roughly proportional to the surface. If n is less than one-third the instantaneous growth rate will be proportional to a power of the weight somewhat greater than two-thirds.

It is also possible to examine the consequences of expressing results in the form of the self-multiplicative growth rate (Minot, 1908), that is, by expressing the weekly or daily growth increment as a percentage of the mean foetal weight during the period concerned. Mathematically this is $\frac{1}{W} \frac{dW}{dt}$ and from equation (6)

$$\frac{1}{W} \frac{dW}{dt} = \frac{a}{nW^n}, \quad (7)$$

but substituting from (5) this becomes

$$\frac{1}{W} \frac{dW}{dt} = \frac{1}{n(t-t_0)}. \quad (8)$$

The elimination of a , the specific growth rate, from equation (8) is additional criticism of the use of this method for expressing foetal growth data. Other reasons why the self-multiplicative method is unsatisfactory in foetal studies have been given by Needham (1931).

SUMMARY

1. During a substantial period of pregnancy foetal development can be adequately represented by a cube-root weight relationship of the form $W^{\frac{1}{3}} = a(t-t_0)$. It is probable that this requires the stable environmental conditions provided by an adequate symbiotic relationship and does not therefore apply to early pregnancy.

2. This formula has two constants peculiar to each mammal: a , which can be regarded dimensionally as a specific growth velocity and can be used to compare the rates of foetal development in different mammals; and t_0 , the intercept on the time axis made by the line through the linear portion of growth.

3. The specific growth velocity a can be approximately determined from birth weight and gestation period data and values obtained in this way reveal remarkable differences between the Primates, sub-Primates and Cetacea.

This work has been carried out with the aid of a grant to one of us (A. St G. Huggett) from the Medical Research Council.

We also wish to thank Dr Richard Phillips of the Department of Animal Health, University College of Wales, for considerable work in providing accurately tugged ewes, and the Great Western Railway for special facilities.

The senior author (A. St G. H.) wishes also to apologize that the same acknowledgement was not attached to the paper by Huggett, Warren and Winterton (1951) on Foetal Blood Fructose in the issue of the Journal, Vol. 113, p. 258, April 1951. It was inadvertently omitted.

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