

any single analytical or "rational" expression for weight. It leads next by way of the numerical evaluation of  $\rho$  to a description of the course of human basal metabolism throughout the same period of life,<sup>3</sup> in terms either of unit or total heat production. Some insight is thus gained into the curious succession of critical points shown in growth and metabolism respectively. This expression for the normal alterations in human metabolism as age proceeds through the period of growth will also serve to define the course of heat production during starvation.<sup>4</sup> In addition, equation (1) may be so arranged to account, at least dynamically, for the nature of the change in weight incident to prolonged fasting, the human case being considered briefly in a succeeding paper.<sup>5</sup> Lastly, equation (1) has been applied to numerous other examples of growth including that displayed by tissue cultures, yeast cells, plants and animals, and in all of these it has succeeded in agreeing with experimental observations. A special example, where, fortunately, simultaneous data on heat production are also available, is considered for the case of bacteria in the final paper of this series.<sup>6</sup>

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**On the Motion of Growth. II. Human Growth in Weight from Early Fetal to Adult Life.**

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The equation of energy previously set forth<sup>1</sup> has been applied to the case of human growth in weight but the steps necessary for this can only be briefly outlined here. We need first to know the nature and relations of the functions  $S, (V_c, E_c)(t)$ , which as already explained, pertain to energy at the source, to that in the form of cells, and to the energy of synthesis respectively. It can be shown that these several factors are connected in the case of "average" human weight by the relation,

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<sup>3</sup> Wetzel, N. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1932, **30**, 233.

<sup>4</sup> Wetzel, N. C., to be published.

<sup>5</sup> Wetzel, N. C., to be published.

<sup>6</sup> Wetzel, N. C., to be published.

<sup>1</sup> Wetzel, N. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1932, **30**, 224.

$$S - \int [V_c + E_c](t) dq = \int [E - E_o e^{-\beta t} \sinh(\theta t - \zeta)] dq + A't \quad (2)*$$

$E$ ,  $E_o$ ,  $\beta$  and  $\theta$  being constants and  $\zeta = \tanh^{-1} \frac{\theta}{\beta}$ . Certain other examples of human growth which depart from the "average" healthy trend, especially between 6-16 years of life have actually proven to be represented instead by an analogous circular function on the right of (2) though this exceptional case will not be treated in detail now. But it is of considerable interest that, whereas neither the hyperbolic nor the circular terms can be omitted in the human case, they vanish for all other examples of plant and animal growth we have so far studied.

The identity (2) is thus seen to symbolize merely the *balance* of energy after that which provides for the cells themselves, and that which is to do the work of synthesis has been deducted from the source. This balance must now suffice to perform three remaining fractions which, together with the energy of synthesis (already discounted), constitute the external work of growth.

Substituting, then, into the equation of energy (1), differentiating once with respect to  $t$ , and transposing terms we get an equation each term of which by these procedures figuratively denotes, per unit of weight, a component in the "forces" of growth:

$$\lambda \frac{d^2 q}{dt^2} + \rho \frac{dq}{dt} + \frac{q}{\kappa} = E - E_o e^{-\beta t} \sinh(\theta t - \zeta) \quad (3)$$

the change in dimension just described being noteworthy. In virtue of (2) it may therefore be seen that equation (3) actually represents the balance of "forces" (and fundamentally, of energy also) remaining to provide on the left for the forces now recognized respectively, as that concerned with the creation and maintenance of the momentum of growth, that required to "overcome" the resistance of growth, and finally that involved in the storage of growth in an environment of permittance,  $\kappa$ .

The foregoing equation has three main integral solutions, accounting theoretically for three outwardly different, though fundamentally identical types of growth, defined in general by the relation,

$$\psi = \left[ \left( \frac{\rho}{\lambda} \right)^2 - \frac{4}{\lambda \kappa} \right] \begin{matrix} > \\ = \\ < \end{matrix} 0 \quad (4)$$

where, as a rule,  $\psi < 0$  in the case of bacterial growth, but where

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\* To facilitate reference the equations in this series of papers are numbered serially.

$\psi > 0$  in human growth. Hence, in the latter, the auxiliary roots are real and negative, and the complete solution of (3) including both complimentary function and the particular integral, becomes by the usual methods, in most compact form,

$$q = E\kappa + D\epsilon^{-\beta t} \sinh(\theta t + \phi) + C_1 \epsilon^{-\alpha_1 t} + C_2 \epsilon^{-\alpha_2 t} \quad (5)$$

the arbitrary  $C$ 's, the  $\alpha$ 's and  $D$  being developed in terms of  $\lambda$ ,  $\rho$ , and  $\kappa$ , in expressions too bulky to be given here, and  $\xi$  being taken up into  $\phi$ .

Now the constants  $\lambda$ ,  $\rho$ , and  $\kappa$ , cannot be themselves obtained from any analysis of growth curves alone. Quite independent relationships are necessary for this,<sup>†</sup> but the computation of values for the human curve in weight can nevertheless be completed as soon as the "combined" constants ( $E\kappa$ ),  $D$ ,  $C_1$ ,  $C_2$ ,  $\alpha_1$ ,  $\alpha_2$ , and the single constants  $\theta$  and  $\phi$  are known, for these may be obtained exclusively from data on growth by a generally applicable method involving the use of least squares subsequently to be described,<sup>2</sup> and are, for our Series XIX:

|             |            |              |          |
|-------------|------------|--------------|----------|
| $E\kappa =$ | 4.397966   | $\alpha_1 =$ | 3.737101 |
| $D =$       | 9.518210   | $\alpha_2 =$ | 0.143894 |
| $C_1 =$     | -11.030331 | $\theta =$   | 0.19     |
| $C_2 =$     | -5.578521  | $\beta =$    | 0.51     |
|             |            | $\phi =$     | 0.217884 |

when  $q$  is expressed in Napierian logarithms. The final figures of all but  $\theta$  and  $\beta$  are rounded.

Of interest is the fact that every step in the calculations, both in deriving the original values just set out, as well as in computing final results for  $q$  or  $z$  at any time  $t$  must be carried through with no less than six, preferably eight to ten significant figures to insure accuracy. The final results for weight, of course, are expressed only to four significant figures, and are set up for various ages in Table I. They are also displayed graphically in Figures (1) and (2) for the ante- and post-natal phases respectively. The former, due to the tremendous change in weight, is drawn semilogarithmically, and shows clearly that relative deviations even in the earliest stages where these tend to be greatest are in reality negligibly small. The data are those of Streeter.<sup>3</sup> For the post-natal phase the ordinary grid is used to avoid confusion in view of the fact that all such

<sup>†</sup> See following paper (III).

<sup>2</sup> Wetzel, N. C., to be published.

<sup>3</sup> Streeter, G. L., Carnegie Institution of Washington Publication No. 274, Contributions to Embryology, 1920, 11, 143.

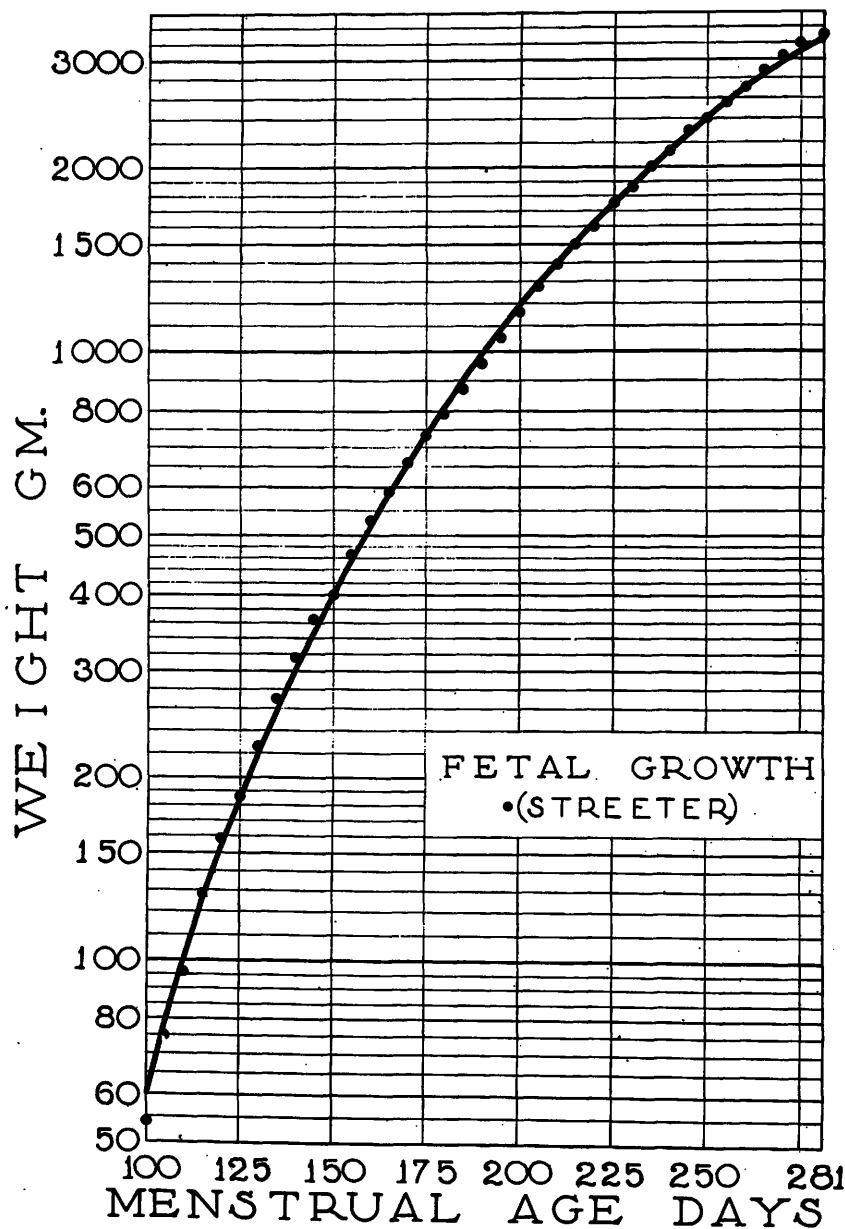


FIG. 1.

The smooth curve displays the prenatal course of growth in weight from the 100th day of gestation (menstrual age) to birth and passes directly through the values computed from equation (5) for this period. The adjustment to the data of Streeter is entirely satisfactory.

TABLE I.

Giving the Numerical Values of Average Human Weight and Rate of Growth as Computed by Means of Equation (5) and its Corresponding Derivatives.

| Age           |               | Weight<br>( <i>z</i> ) | Rate of Growth      |                 |
|---------------|---------------|------------------------|---------------------|-----------------|
|               |               |                        | $dq/dt$             | $dz/dt$         |
| Menstrual Age | 100 days      | <i>Kg.</i>             | <i>Kg./Kg./year</i> | <i>Kg./year</i> |
|               | 125 "         | 0.069                  | 16.0539             | 1.108           |
|               | 150 "         | 0.185                  | 12.6366             | 2.338           |
|               | 175 "         | 0.400                  | 9.9786              | 3.992           |
|               | 200 "         | 0.736                  | 7.9091              | 5.821           |
|               | 225 "         | 1.194                  | 6.2960              | 7.517           |
|               | 250 "         | 1.757                  | 5.0367              | 8.850           |
|               | 281 " (Birth) | 2.396                  | 4.0520              | 9.709           |
|               |               | 3.251                  | 3.1208              | 10.146          |
| Legal Age     | 6 mos.        | 7.565                  | 0.8667              | 6.559           |
|               | 1 yr.         | 10.062                 | 0.3788              | 3.813           |
|               | 2 yrs.        | 12.695                 | 0.1569              | 1.993           |
|               | 3 "           | 14.192                 | 0.0913              | 1.296           |
|               | 4 "           | 15.486                 | 0.0876              | 1.356           |
|               | 6 "           | 18.852                 | 0.1095              | 2.064           |
|               | 8 "           | 23.759                 | 0.1186              | 2.818           |
|               | 10 "          | 29.967                 | 0.1115              | 3.342           |
|               | 12 "          | 36.917                 | 0.0963              | 3.555           |
|               | 14 "          | 44.000                 | 0.0792              | 3.485           |
|               | 16 "          | 50.712                 | 0.0630              | 3.195           |
|               | 18 "          | 56.709                 | 0.0492              | 2.790           |
|               | 20 "          | 61.850                 | 0.0380              | 2.350           |
|               | 22 "          | 66.030                 | 0.0292              | 1.928           |
|               | 24 "          | 69.510                 | 0.0221              | 1.536           |
|               | 32 "          | 77.316                 | 0.0072              | 0.557           |

curves have become well known in this form. The field through which the theoretical curve for healthy weights passes denotes the limits of what can actually be accepted as "normal average" in the collected and well-known observations of Camerer, Czerny-Keller, Pirquet, Woodbury, Baldwin, Boas, and others.†

The agreement, for the purpose in view, namely, a reproduction of the trend of healthy human growth throughout the entire life cycle is wholly satisfactory, notwithstanding the rather remarkable span over which equations (1-5) hold true. They may, accordingly, be confidently trusted even in this instance, which, so far as we are aware, undoubtedly represents the most complicated example of growth. They are, finally, of sufficient generality to be applied, if desired, in similar ways to the case of "individual" growth curves.

† The recent excellent data of Gray and Ayres\* follow the upper limit of this field faithfully.

\* Gray, H., and Ayres, J. G., *Growth in Private School Children*, Chicago, University of Chicago Press, 1931.

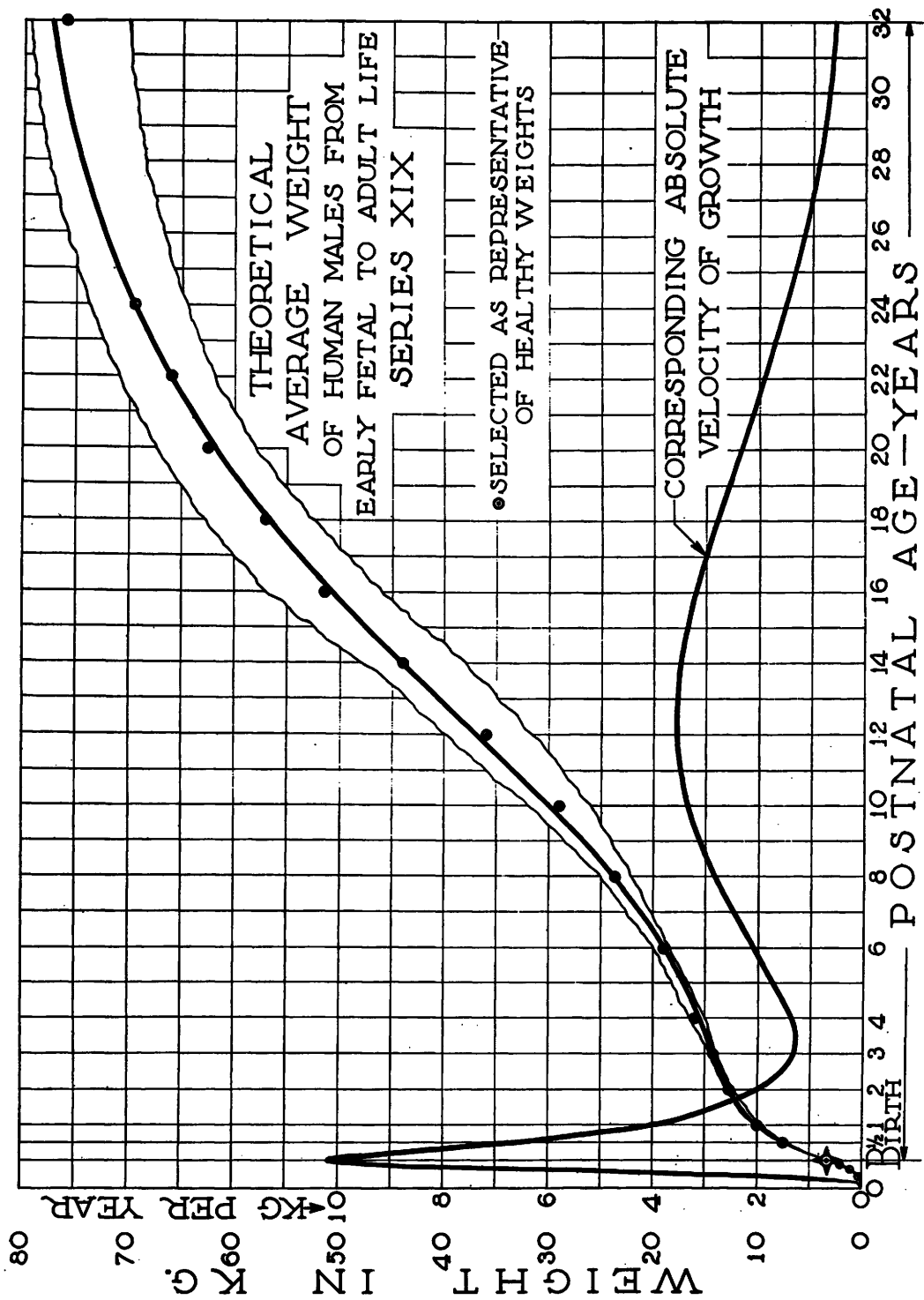


Fig. 2.

The smooth curve is drawn through the values computed directly from equation (5). It redescribes satisfactorily the "ideal" course of growth indicated by the points chosen as representative of healthy weights from early prenatal throughout late postnatal life. The former phase is displayed greatly magnified in Fig. 1. The surrounding white field would contain 98% of all data available for healthy subjects, the latter for certainty of the smaller range.