PROBABLY the greatest contributions to successful artificial feeding of infants that will ever be witnessed have already been made, namely: the discovery of the importance of bacterial contamination; the recognition of the role of vitamins; and the realization that fresh cow's milk produces large curds in the infant's stomach and must be treated by heat or other means to improve its digestibility.

Elimination of these major handicaps of artificial feeding permitted attention to be focused on determination of precise figures for the amounts of individual nutrients which should be supplied by the diet to foster sound nutrition. Special interest was attracted by the question of the relative adequacy of the protein in cow's milk and human milk. This called for refinement in methods of appraising the state of nutrition and clarification of the ultimate goal in infant feeding—the most desirable state of nutrition.

Premature or excessive emphasis on selection of a figure for the dietary allowance of a nutrient is liable to arouse emotional controversy and distract nutritionists from the fundamental issues involved in judging nutritional status. Progress in the science of nutrition could easily be hampered by satisfaction with the sort of pseudosophistication so readily conveyed by plain numbers.

If a figure for an allowance is proposed, there is a great temptation to exploit such a handy value by matching the composition of food products against this kind of "standard." The clamor of conflicting claims in the market place threatens to obscure the deficiencies in the fundamental knowledge upon which a meaningful figure for the allowance of protein or any other nutrient must be based.

The Food and Nutrition Board of the National Research Council has now wisely recognized these considerations by not including a figure for protein allowance in

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ADDRESS: Babies Hospital, 3975 Broadway, New York 32, New York.
infancy in the 1958 revision of their *Recommended Dietary Allowances* which states: "Breast-feeding is the best and desired procedure for meeting the nutrient requirements in the first months of life."

This is a favorable setting in which to survey the principles which should govern the determination of the dietary allowance of protein for infants and to dwell upon the significance to be attached to any value proposed. The time has come to shift emphasis from the choice of a figure per se to the central problem in nutrition—correlation of nutritional status and performance of the individual with dietary intake of nutrients.

**TELEOLOGY AND SCIENCE IN NUTRITION**

If we intend to give any thought to the matter, it would be absurd to yield to the attractive simplicity of accepting Nature's food as best simply because in the course of evolution the human race was able to survive infancy on this fare. When man lived naturally, in the sun and by instinctive choice of natural foods, it may have been safe to assume that mother's milk was adequate to serve as the sole food in early infancy. In the unnatural life of civilization, it has already been necessary to abandon this assumption; now the breast-fed usually need supplementary vitamin D, and perhaps ascorbic acid and iron. It can no longer be considered sacrilege to question the perfection of Nature.

Because one fault is discovered, it does not follow that there must be other deficiencies in the milk of modern mothers. But now teleologists must defend their position with evidence, not wistful faith, nor should they resort to intellectual nihilism or plausible platitudes. Artificial living may necessitate artificialities in the diet, but each departure from Nature must be thoroughly justified.

Neither are there grounds for complacency in scientific nutritionists, for their contributions to date have not outmoded the pithy comment of Oliver Wendell Holmes:

A pair of substantial mammary glands has the advantage over the two hemispheres of the most learned Professor's brain, in the art of compounding a nutritious fluid for infants.

The fact is: we are woefully ignorant as to the best means of nourishing an infant. There is no place for dogmatism, emotional controversy or promotional fervor in discussions of the protein allowance.

The following discussion reflects the difficulties in discerning the true meaning in the communications of the scientists, if one does not accept the comfortable faith of the teleologist.

**OPTIMAL NUTRITION**

It is generally considered more admirable "to eat to live" than "to live to eat." The cultural aspirations of civilized man have to do with creativity and happiness, with the artistic and the spiritual—not with mere survival and sensual contentment or acquisition of material bulk and brawn. The ultimate social implications of nutrition must be expressed qualitatively before they can be quantitated.

If nutritionists seek a more significant role in society and wish to help civilized man realize his aspirations, then they must face the indispensable task of examining the relation between a given state of nutrition and the behavior and achievements of the individual. From this viewpoint the "optimal" or "correct" state of nutrition is a philosophic and cultural concept—optimal for what? Do we seek the best diet for material achievement—through maximal growth (Size), freedom from disease (Health), postponement of death (Longevity), fitness for work and war (Strength and Endurance), survival (Reproduction)? Or do we have more concern for the relation of diet to cultural achievement—through function of the mind (Thought), behavior (Social Relations), emotional well-being (Happiness)?

The pertinence of scientific measurements directed at estimating optimal nutrition depends on the definition of "opti-
The preoccupations of scientific nutritionists at any time may be directed as much by the limitations of available techniques as by current concepts or attitudes. Until recently, measurement of external dimensions of the body and use of balance studies to determine retentions of nutrients in the body have been the principal endeavors, other than the detection of signs of deficiencies. The relevance of the findings from these techniques to the cravings of civilized people may be remote.

The chief purpose of stating specific quantities of nutrients as dietary allowances is to guide the formulation of diets which will foster an acceptable state of nutrition. And so one always returns to the more fundamental problems: defining the goals of nutrition and assessing the results of dietary practices.

To contrive a definition of optimal nutrition, even within the restricted terms of the material aspects of man's performance, presents formidable obstacles. One ambitious attempt resulted in the exuberant statement (italics mine):

Optimum nutrition (is) that which provides all dietary nutrients in respect to kind and amount, and in proper state of combination or balance so that the organism may always meet the various exogenous and endogenous stresses of life, whether in health or disease, with a minimal demand or strain on the body's natural homeostatic mechanisms.³

It is obvious that this definition places emphasis on survival and opens the way for the troublesome set of obscure notions of "stress" and "strain." This definition also introduces a concept of nutrition which calls for carrying a load of "insurance" or "reserves" to be ready "always" for the possible "stresses," at a premium of unknown cost to the organism. At least the philosophy behind this definition conceives the functional capacity of the organism to be of greater importance than its size or composition.

A more restrained though equally vague statement, which calls for appraisal of the state of nutrition in terms of functional performance, may be proposed: An acceptable state of nutrition will enable the organism to enjoy full exercise of its natural functions and resist harmful conditions; the best diet will achieve this without subjecting the organism to an excessive or detrimental metabolic task. In order to select such a diet, it will be necessary to relate the composition of various diets to the states of nutrition achieved, separate from all other factors which may affect performance of an organism. This relation may be investigated directly, by measurements of functional capacity, or indirectly, by means of indices such as growth and development and health. This undertaking is sufficient to occupy nutritionists for the foreseeable future. Perhaps ultimately the imponderable relation of maximal to optimal nutrition could be explored more profitably, and efforts to improve on Nature would not seem so presumptuous and questionable.

GENERAL CONSIDERATIONS GOVERNING DIETARY ALLOWANCES

Major obstacles to stating a figure for the dietary allowance of a single nutrient like protein, often overlooked or ignored, are the variability of individuals and the simple fact that the nutrient is not fed alone in a pure form. Practical circumstances demand that the nutrient under study shall always be fed as part of a complex mixture; the results reflect the influence of all constituents of the diet. The amount of protein which a particular diet contains can be properly related only to the performance of members of the particular species employed, in circumstances prevailing during the observations. It is unreasonable and hazardous to conclude that the amount or proportion of protein contained in one complex diet can be readily expressed as a general statement of the allowance which other diets should provide to achieve similar performance from different subjects or other species. The effects of the protein component of the diet are greatly influ-
enced by the peculiarities of the individual and by other aspects of the diet, for example: caloric value; percentage composition of fat, carbohydrate and protein; content of essential vitamins and minerals; digestibility and efficiency of utilization; etc. With natural foods the content of protein in the diet cannot be varied without affecting other characteristics of the diet.

Thus a figure for the desirable allowance of a single nutrient must be viewed as essentially an abstract notion—it must not be assumed to have the attributes of a fundamental constant. Actually, as one must depend upon a complete diet, more realistic statements of allowances might be expressed in terms of amounts of the available foods which a proper diet should include in order to support a desired state of nutrition. The opportunities for error in constructing a diet by using figures for allowances of specific nutrients and a table of composition of foods must be discouraging to a thoughtful dietician.

The question of dietary requirements in practical feeding in early infancy might be resolved by determining the amount of a milk product and supplementary vitamins that would enable the infant to reach current expectations for sound performance. This question must be answered for each product individually and the results with one diet cannot be dependably transposed to judge the adequacy of any other product.

APPRAISAL OF STATE OF NUTRITION

What progress has been made in selecting indices for appraisal of the state of nutrition? How satisfactorily can the existing indices be applied? What are the limitations in these indices?

Throughout this discussion the comments pertain to nutrition of normal infants, particularly in the first 6 months of life; no consideration is given to the extent to which they are applicable to premature infants or abnormal infants.

Up to the present time, the principal approaches to evaluation of nutritional status of infants, as far as its relation to physical achievement is concerned, have been based on measurements of growth.

Outer Aspects of Growth

BODILY DIMENSIONS: A superficial glance at the finished appearance of charts for plotting the length and weight of infants in relation to age, and the massive accumulation of anthropometric data, tend to create the impression that assessment of the state of nutrition by physical growth is on a firm basis. Tanner4 and McIntosh5 have recently surveyed the present position of assessment of growth and development. Unfortunately, it appears that laborious effort by devoted workers over the past 75 years has not provided an “ideal” reference for quantitative comparison of the physical size attained by groups consuming different diets. Moreover, the size observed at a given time (distance achieved) gives no clue as to the rate of growth (velocity). The evaluation of the nutritional status of an individual in terms of rate of physical growth is especially crude.

Averages derived from populations of the same age (cross-sectional data) cannot be employed to judge the progress of an individual, i.e., whether suitable increments in growth have accrued in successive intervals of observation (longitudinal data).

In actual practice the crucial questions are: Has a particular infant grown to reach a size prevalent in a healthy population? Is he growing at a normal rate? How accurately can his growth be compared to that of other individuals or groups within these frames of reference? How large are the deviations in healthy populations and individuals, in size at a given age and in rate of growth?

Even if attainment of maximal physical growth should be accepted as the criterion for an optimal diet, the evaluation of this in individual infants would be frustrating because “the size of the newborn baby is
only very slightly related to the size of the adult, or even to the size of the 2-year-old" and ". . . the rate of growth from birth to 5 years has only a very small effect on adult measurements. Rate and size seem practically independent."6

This is simply because the rate of growth after birth is not dependent upon the diet alone—prenatal factors, such as maternal nutrition, size of the uterus and placenta, and heredity, are also influential. The genetically determined rate of growth may have been deflected during fetal life, and time will be required after birth to resume the genetically determined curve, usually not until between 1 and 2 years of age. This was demonstrated especially clearly in a longitudinal study by Falkner,7 in which it was found that for 124 subjects the correlation coefficient between recumbent-

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Figs. 1-4. Weight-age relationships of individual boys, plotted on Iowa Growth charts for boys, 1) Breast-fed (Paiva8); solid line is median of all boys in this study. 2) Cow's milk, high protein intake (Jeans and Stearns'). 3) Human milk (Fomon et al.'). 4) Cow's milk, intermediate protein intake (Fomon et al.'). The Iowa Charts give curves for the median and 16th and 84th percentiles of different groups of infants at the various ages (cross-sectional data) and do not depict the growth of a single group of infants followed serially from birth (longitudinal data).9 (See discussion in text.)
lengths of infants at 4 weeks and 1 year was 0.30 (little relationship) while between infants at 1 year and 2 years it was 0.83 (close relationship).

This means that during infancy the plot of the growth of an individual against age may drift across the curves depicting averages and deviations from means of bodily dimensions characterizing a group without this being necessarily an indication of growth failure or precocity of the individual or a reflection of the inadequacy or superiority of a diet. This is illustrated in Figures 1 through 4 constructed from data on individual subjects in three papers concerned with metabolic balance studies and one paper on the growth of breast-fed infants: the growth of all of these infants is within normal limits.

This elementary material is reviewed as a reminder that it is fallacious to compare the adequacy of diets for infants on the basis of growth of individuals or the averages of small groups. Significant comparison of the effects of different diets on growth requires proper conduct of carefully controlled observations with sufficient numbers of subjects to make due allowance for the play of chance. Metabolic balance studies of infants are usually designed to provide information on the retention of nutrients during brief periods by a few subjects; even when the growth of the subjects is judged to be normal, their dimensions cannot be treated as if obtained from a proper study of growth, and comparisons of growth of small groups from such studies are not proper.

Even though the milk secreted by mothers is subject to considerable fluctuations in composition, it seems reasonable, until better criteria are proposed, to use the growth of a large number of normal infants fed at the breasts of healthy mothers (and who are given supplementary vitamin D) as an appropriate reference for comparing the results of other means of nourishing infants. It should be embarrassing to nutritionists, and may come as a shock to many pediatricians, to learn that amazingly few data have been gathered from infants fed exclusively with human milk during the first 3 to 6 months of life.

None of the better studies of growth of breast-fed infants found in the literature provides sufficient suitable data for construction of reference charts for appraisal of growth of infants fed by artificial means. Each of these series of breast-fed infants suffers from one or more limitations: supplementary cow’s milk or solid foods were also given; too few subjects; infants with illnesses were included; short period of observation; only mean values for weight or height were reported; bias in the selection of sample of population; etc. It is of some interest that the means of the weights from birth to 6 months of age were quite similar in four series of breast-fed infants reported in 1898, 1927, 1931, and 1953.

It can be seen in Figure 1 that the curve depicting the median for growth of the breast-fed group in the 1953 series approximates the similar curve for the general infant population in the same region which included many infants reared on cow’s milk formulae. This suggests that, under modern conditions, the rate of gain in weight of breast-fed and artificially fed groups of infants may not be different, but this obviously does not constitute an adequate comparison. This series of breast-fed infants comprised only 21 males and 24 females and they were fed human milk exclusively for only the first 3 months of life.

It is evident that there is considerable need for additional data before we will be in a satisfactory position to evaluate the state of nutrition of infants, determine the dietary allowance of a nutrient or judge the adequacy of various diets, even by the simple measurement of height and weight. The recent trend to collect longitudinal data from individual infants as a means of developing standards for velocity of growth may improve the situation, but it will be desirable to make such observations on in-
fants being fed exclusively at the breast to provide a basic reference for nutritional studies.

Not only are the standards for appraising growth unsatisfactory, but bodily growth during early infancy is too much affected by many factors to serve as a specific index of the effect of diet on nutrition. Enumeration of a few such factors should suffice to indicate that physical growth of infants must be used critically and cautiously as a means of comparing the nutritional states achieved by diets, e.g.: hereditary influences, prenatal factors, metabolic peculiarities in the individual, infection, etc.

Above all else, it must be constantly kept in mind that over-all measurements of body size cannot reveal the body composition or qualitative behavior of the subject—physical dimensions cannot be coupled with an assumption that bigger is better.

Norms, standards and ranges of values are the products of measurement of groups of children (and depict the distribution of the measurements and the central tendencies). Clinically, the problem is to evaluate the individual child who is entitled to realize his optimal rate of growth and ultimate size according to his own potentialities.

Inner Aspects of Growth

Metabolic Balance Studies: A time-honored technique for collecting information on nutrition is to determine the retention of nutrients in the body by measuring the balance between intake and output of a substance or some representative fragment. The material retained is assumed to be incorporated into the tissues. The amounts retained can be correlated with total weight gain or other aspects of the subjects and the effects of various diets on these can be compared.

Advantages of this technique over gross body measurements are: the magnitude and rapidity of change in retentions may permit evaluation in a shorter time than would be required to note effects on over-all dimensions of the body; more rigid control of the subject is possible during convenient short-term observations; the influence of factors, e.g., heredity, requiring a long time to produce their effects, is minimized; relatively few subjects may be sufficient to provide significant results; the same subjects may be used to make a series of comparisons of different diets, thus avoiding the effect of variations between individuals; the subjects are under close scrutiny of the investigators throughout the periods of observation.

The balance technique has serious limitations: the collection of specimens, measurement of intake and the chemical analyses demand tremendous care and effort to achieve accuracy; much skill and experience are needed in every step; the expense involved to maintain the special facilities required is almost prohibitive; suitable subjects are difficult to obtain and to keep in a metabolic unit for observation under conditions acceptable as normal; for some nutrients the amount retained may be such a small percent of the total intake as to require extreme precision to prevent a degree of error which would jeopardize the significance of the balance; cumulative error in apparent retentions is difficult to detect; no information is given as to the locus of deposition of the retained material or its migrations within the body; losses from the integument or in sweat may be considerable and are difficult to measure.

In spite of these obstacles, accurate and informative data can be accumulated from balance studies of infants consuming diets composed of various kinds and amounts of protein. Because of the special problems presented by collecting human milk and feeding it to infants as the diet during balance studies, little basic information on retention of nitrogen by infants fed human milk has been published. The Borden Award for 1958 was assigned to the author partly for his role in facilitating the accumulation of data in this area—so fundamental to evaluation of artificial means of feeding infants. The project would not have succeeded if the interest of Dr. Samuel Fomon had not been aroused, for it was his
superior investigative ability and attractive personality that were responsible for the quality and magnitude of the data. The results should go a long way toward filling a serious gap in the knowledge essential to sound practice in infant feeding.

In the studies by Fomon and May the infants fed human milk ad libitum had a mean intake of protein during the first 1% months of life of 2.4 gm/kg/day and 1.5 gm/kg/day between 4% and 6 months; corresponding mean retentions of nitrogen were 183 mg and 69 mg/kg/day, respectively. With ad libitum provision of a formula of cow's milk containing intermediate amounts of protein, the infants' average intake of protein was 3.3 gm/kg/day during the first 1% months of life and 2.5 gm/kg/day between 4% and 6 months; corresponding mean retentions of nitrogen were 211 mg and 102 mg/kg/day, respectively.

The infants studied by Jeans and Stearns and co-workers were fed considerably greater intakes of protein (generally more than 3.5 gm/kg/day) and larger retentions of nitrogen were reported. Calculations from their data show the mean retention of nitrogen at 7 weeks of age was 174 mg/kg/day and at 6 months of age it was 125 mg/kg/day. (No infants studied younger than 7 weeks.)

There are only a few balance studies comparing the results when infants were fed the same quantity of protein from human milk and cow's milk; in these the close equivalence of the protein from these two sources for infant nutrition was apparent as far as retention of nitrogen is concerned.

Within the range of intakes of protein supplied by the feedings in the balance studies mentioned, it may seem as if the greater the intake of protein the larger the retention of nitrogen. This possibility is the subject of special consideration later in this essay. The intermediate amounts of protein supplied from cow's milk (3.3 to 2.5 gm/kg/day) resulted in retentions of nitrogen as large, or greater than, those obtained with human milk.

It has already been pointed out that, although the growth of the infants in all these studies was within the range of normal, the growth data are not adequate to compare the growth performance of the groups fed the different intakes of protein from human and cow's milk. Complementary observations of the growth of larger groups of infants, consuming the milk products alone, will be required for a definitive comparison.

It has seemed mysterious that the large retentions of nitrogen reported with the high intakes of cow's-milk protein fed to the infants studied by Jeans et al were not accompanied by greater growth than that of breast-fed infants. Even if this finding was not problematic it would not justify an assumption that retentions of nitrogen greater than those induced by feeding human milk are advantageous. In the following section on Body Composition it will be shown that the magnitude of the larger retentions would ultimately result in an inordinately high percentage of nitrogen in the body composition—in fact a percentage which is theoretically unlikely and not in keeping with data from actual chemical analysis of the bodies of infants.

It should be evident that balance studies with cow's milk do not provide a completely adequate basis for stating the proper dietary allowance for protein; nevertheless the studies of Jeans et al have been employed with great emphasis by advocates of the liberal allowance formerly proposed by the National Research Council. This should not be construed as disparagement of the extensive careful studies by Jeans and co-workers, but it may be recalled that their investigations were not designed to determine the protein allowance. Reference to the original papers discloses that the studies were undertaken to appraise the effects of various treatments on the curdling of milk and the suitability of evaporated milk for infant feeding, at the time the product was first being proposed for this purpose. The level of protein intake supplied in Jeans' studies reflected current practice, and different levels were not com.
ALLOWANCE OF PROTEIN

pared. Any unwarranted extrapolation of the findings in these investigations should not be charged to Jeans, who near the end of his career stated his own opinion to be: . . . the protein of human milk is not superior to that of cow's milk, contrary to the concept we have held for so long and on which we have based feeding practices. 23

**Body Composition:** It was inevitable that thoughtful investigators would seek better means of appraising nutritional status, particularly through studies of the actual composition of the body resulting from various dietary intakes of nutrients. The concentrations of constituents in the circulating blood give little insight into the composition of the body, and are likely to be maintained at normal levels at the expense of the tissues. Measurements of these are more apt to reveal gross deficiencies than to serve as a means of appraisal of relative adequacy of diets, especially where only minor differences exist.

Meat packers could not escape an interest in the relation of diet to composition of the animal. Stock raisers have long been concerned with efficiency of utilization of feeds and the qualitative nature of the weight gained. Their curiosity can be satisfied by direct analyses of an unlimited supply of carcasses.

Although there appears to be renewed interest on the part of students of human nutrition in the factors influencing the composition of the body, exploration of the matter began long ago. The basic concepts now being pursued were developed in a stimulating paper by Moulton in 1923, 21 and in 1945 were employed by Mitchell and co-workers 25 to clarify the problem of determination of dietary requirements of nutrients. The thesis presented in the introduction to the paper by Mitchell et al. 26 can be given best in their own words:

The amounts of nutrients contained in the adult human body represent the integration of the day to day accretions from the time of conception to the termination of growth. These accretions are usually determined by balance experiments carried out at different periods of growth and are assumed to measure the net requirements of the respective nutrients with due consideration of the synthesis and transformation of organic nutrients in metabolism. Thus, the accretion of fat does not measure a fat requirement, but the accretion of protein and of the essential mineral elements may. Whether it does or whether it does not, will depend upon the capacity of the body to store the nutrient in amounts considerably greater than current needs. . . .

The extent to which metabolic balances of nitrogen, calcium, iron, etc., actually measure the day to day requirements in terms of net nutrients can be judged by comparing their total integration throughout growth with the composition of the mature body with respect to them. However, information on the composition of the adult human body is strangely contradictory and incomplete.

In spite of the slaughter in wars and the carnage of the highways, the body of a human, normal at the time of death, is seldom available for chemical analysis; and only rarely could one expect to obtain the body of a normal infant. A haphazard collection of bodies of a few infants for chemical analysis could never permit sufficient correlation with diets to serve as a dependable approach to appraisal of the nutritional states promoted by different diets.

The unavoidable handicaps in obtaining data by direct analyses of human bodies for comparison with dietary intakes of nutrients has stimulated search for methods of indirect estimation of body composition in the living. The available methods and the many complicating problems were reviewed recently 26 and it was stated: "There are, in fact, no adequate methods for complete in-vivo analysis, and there are, moreover, none in sight." Water is the only constituent amenable to direct measurement in vivo; fat may be estimated by indirect means and protein and minerals are lumped together as fat-free residue and the quantity inferred by subtracting total water and fat from body weight.

Because of the dearth of suitable bodies for dependable direct analyses and the limitations of indirect determinations in the
living, a critical estimate of the probable contribution of studies of body composition to the appraisal of the state of nutrition in relation to diet should be made before this approach is pursued too hopefully.

Because of the apparent universality of principles governing the nature of growth in a wide assortment of species, a great deal may be inferred from studies of the effect of diet on the body composition of animals. Moulton elaborated upon the concept of the constancy of the composition of the fat-free components of the body and pointed out the independence of this composition from the amounts of essential nutrients in the diet, once a state of "chemical maturity" has been reached—when the percentages of water, protein and salts in the body become comparatively constant, calculated on a fat-free basis. This state is reached at approximately the same stage in the life-cycle of most species; at 50 days of age in the rat and estimated as between 2 and 3 years of age in man. The constituents of diets influence the rate of growth and the ultimate size, but variation in composition of the body will be restricted to the percentage of fat accumulated, after chemical maturity is attained. These statements are supported by data from analyses of human bodies and from studies of the body composition of rats fed diets providing extreme variations of protein intake (Tables I, II and III).

As already indicated in the section on Outer Aspects of Growth, during the first year of life, infants exhibit profound adjustments in growth as they recover from deflections of the genetically determined pattern of growth induced by prenatal factors. This fact and the delay in reaching chemical maturity until 2 years of age or later probably preclude precise correlation of body composition and diet in the period of infancy, unless observations could be made on identical twins.

**Implications of Studies of Body Composition**

**Body Composition and Nitrogen Balance:** Reference has already been made to the enigma presented by the large reten-

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**TABLE I**

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight (gm)</th>
<th>% Wet</th>
<th>% Fat-free</th>
<th>% Wet</th>
<th>% Fat-free</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>3.5 kg</td>
<td>12.0</td>
<td>14.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td>45.0 kg</td>
<td>14.4</td>
<td>19.2</td>
<td></td>
<td></td>
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</tbody>
</table>

**TABLE II**

<table>
<thead>
<tr>
<th>Protein in Diet</th>
<th>Age (days)</th>
<th>Weight (gm)</th>
<th>Protein</th>
<th>Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>% Wet % Fat-free</td>
<td>% Wet Weight</td>
</tr>
<tr>
<td>18%</td>
<td>42</td>
<td>147.1</td>
<td>16.5</td>
<td>18.4</td>
</tr>
<tr>
<td></td>
<td>110</td>
<td>350.3</td>
<td>19.3</td>
<td>21.4</td>
</tr>
<tr>
<td></td>
<td>230</td>
<td>439.2</td>
<td>17.7</td>
<td>18.7</td>
</tr>
<tr>
<td>35%</td>
<td>42</td>
<td>161.9</td>
<td>16.6</td>
<td>19.3</td>
</tr>
<tr>
<td></td>
<td>110</td>
<td>445.9</td>
<td>16.2</td>
<td>20.5</td>
</tr>
<tr>
<td></td>
<td>230</td>
<td>540.9</td>
<td>15.8</td>
<td>21.5</td>
</tr>
</tbody>
</table>

* From Pickens et al.
TABLE III

Effect of Diet on Body Composition: Rats Fed Sufficient Amounts of Diets of Various Protein Contents to Achieve Equal Gains in Weight (Pair-feeding)*

<table>
<thead>
<tr>
<th>Protein Content of Diets</th>
<th>4% vs. 8%</th>
<th>8% vs. 12%</th>
<th>10% vs. 20%</th>
<th>20% vs. 54%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total gain (gm)</td>
<td>42.5</td>
<td>43.5</td>
<td>188.0</td>
<td>189.9</td>
</tr>
<tr>
<td>Protein in weight gain (%)</td>
<td>20.6</td>
<td>24.4</td>
<td>19.1</td>
<td>20.4</td>
</tr>
<tr>
<td>Total protein gained (gm)</td>
<td>8.75</td>
<td>10.83</td>
<td>36.0</td>
<td>38.6</td>
</tr>
</tbody>
</table>

* From Hamilton.29

The data in Table III show that for each gram of nitrogen (6.25 grams of protein) retained, the mean gain in weight was 27 grams. This would mean that the weight gain was composed of about 23% protein—obviously out of keeping with information on body composition. (Calculations from the observations of an infant selected at random from one of Jeans' experiments are shown in Table IV.) If the data on body composition were to be considered more dependable, it could only be surmised that some cumulative error in balance studies of this type leads to false inferences regarding the quantitative composition of weight gain produced by high intakes of cow's-milk protein.

The infants fed human milk by Fomon et al.9 gained 42 grams in weight for each gram of nitrogen (6.25 grams protein) re-

TABLE IV

Calculations from Nitrogen Balance Studies of an Infant* Receiving a High Intake of Cow's-milk Protein

<table>
<thead>
<tr>
<th>Age at Study (weeks)</th>
<th>Weight (gm)</th>
<th>Nitrogen</th>
<th>Intake (gm/kg/day)</th>
<th>Retention (gm/kg/day)</th>
<th>Retention×Wt. (gm/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>5,000</td>
<td></td>
<td>.673</td>
<td>.252</td>
<td>1.29</td>
</tr>
<tr>
<td>11</td>
<td>5,670</td>
<td></td>
<td>.552</td>
<td>.187</td>
<td>1.12</td>
</tr>
<tr>
<td>13</td>
<td>5,965</td>
<td></td>
<td>.630</td>
<td>.172</td>
<td>1.03</td>
</tr>
<tr>
<td>15</td>
<td>6,360</td>
<td></td>
<td>.583</td>
<td>.161</td>
<td>1.02</td>
</tr>
<tr>
<td>18</td>
<td>6,980</td>
<td></td>
<td>.558</td>
<td>.143</td>
<td>1.00</td>
</tr>
<tr>
<td>22</td>
<td>7,515</td>
<td></td>
<td>.589</td>
<td>.252</td>
<td>1.80</td>
</tr>
</tbody>
</table>

Days observed = 90. Weight gained = 2,425 gm.
Average protein intake = 3.84 gm/kg/day (N×6.25).
Average protein gain = 6.65 gm/day (N×6.25).

Total protein gained (6.65 gm×90) = 618.5 gm

Total weight gained (2,425 gm) = 2,425 gm

(Compare with values for body composition in Table I.)

* Baby Awe, page 76 in the paper of Jeans and Stearns.8
tained, which gives a figure of 14.8% for the protein component of the weight gain—a reasonable figure. In other studies by Fomon et al. infants fed slightly greater amounts of cow’s-milk protein than was consumed by those fed human milk gained 33 grams for each gram of nitrogen retained, giving a composition of 18.8% protein in the weight gain—all a figure which could be taken to suggest cumulative error in balance studies with intakes of protein from cow’s milk slightly higher than received by breast-fed infants.

It may seem that studies of body composition create doubt as to the significance of the retentions of nitrogen calculated from data obtained from balance studies with cow’s milk, but these considerations especially warn against acceptance of the claim that progressive increase in retention of nitrogen with increasing intake of protein indicates a consequent progressive increase in the percent of protein in the body composition.

A source of cumulative error in these nitrogen balance studies has not been demonstrated. Perhaps there are defects in the chemical methods employed. With the higher intakes of protein there may be excessive losses of nitrogenous substances from the skin and in sweat or even in gaseous form from the lungs; these are not measured in the usual balance technique and are not included in the calculations of retentions. The nonprotein nitrogenous constituents in human and cow’s milk may behave differently in these respects (the nonprotein nitrogenous constituents, ammonia, urea, amino acids, etc., make up 17% of the total nitrogen of human milk and 6% of the total nitrogen of cow’s milk).

Nitrogen balance studies using higher intakes of human-milk protein than received from the breast, i.e., breast-milk fortified with human-milk protein, have not been done. This would be a way to further test the validity of the nitrogen balance technique.

Percentage Composition versus Total Content: Two important considerations must be kept in mind to avoid misapplication of the data from studies of body composition to the determination of dietary allowances of nutrients. First, the percentage of protein in the fat-free component of the body does not become constant until the age of “chemical maturity” is reached, estimated at between 2 and 3 years in man. Second, the expression of the composition in percentages must not be allowed to obscure the actual amounts of protein deposited in the body during periods of growth with different diets.

From the first consideration, it may be deduced that the percentage of protein in the increment of weight gained must surpass the percentage in the whole body at the time, until the fixed composition and maximum protein content of the tissues characteristic of the adult prevail. This may be more readily comprehended with the aid of the following calculations based on data in Table I:

**Rat**

Newborn: weight 6.23 gm, 9.01% protein = 0.6 gm protein in body.
14 days: weight 22.3 gm, 13.24% protein = 2.9 gm protein in body.
Weight gained = 16.07 gm. Protein gained = 2.3 gm; 14.3% of gain.

**Human**

Newborn: weight 3.5 kg, 12% protein = 420 gm protein in body.
1 year: weight 10.5 kg, 15% protein = 1,575 gm protein in body.
Weight gained = 7,000 gm. Protein gained = 1,155 gm; 16.5% of gain.

However, it may be noted that the composition of the gain in the example shown in Table IV greatly exceeds reasonable expectations.

In experiments with rats (Tables II, III), it was shown that widely varying intakes of protein resulted in approximately the same percent of protein in the fat-free portion of the carcasses or the weight gained, but the growth and the total deposition of protein were quite different. As the percent of protein in the diet increased from 4% to between 12 and 16%, growth and the amount of protein deposited increased, but further in-
crease in dietary protein beyond 16 to 54% resulted in poorer growth and no greater deposition of protein. Although the ages of these rats correspond to the period of adolescence rather than infancy in the human, the results reveal general characteristics of any period of growth.

Thus it is evident that the actual gain in protein in the body, as well as the total weight gain, is influenced by dietary intake. Studies of body composition will prevent preoccupation with over-all size, but they will also leave the fundamental problem in appraisal of nutrition as it was—to relate the size of the body and its content of protein and other constituents to the physiologic performance of the organism. In other words, studies of body composition, like anthropometric measurements, give anatomic or morphologic information—all mere quantities—which should not arrest the attention of nutritionists unduly unless they can be related to functional capabilities. The basic questions of health and the aims of nutrition can be dealt with only in this fashion.

The Concept of Protein Reserves: The concept of provision of an abundant intake of protein to stock the organism with “reserves” to meet possible “stress” from disease or periods of deprivation has governed the aims of some nutrition enthusiasts and has influenced statements for the dietary allowance of protein.

One example of the manner in which the concept of “reserves” can be employed is derived from the classic investigations of Whipple and co-workers on the fabrication of serum proteins. It was discovered that restoration of serum proteins in animals, depleted by plasmaphoresis, was dependent upon the nutritional state of the animal and the amount and quality of the protein provided in the diet. A sizeable portion of the protein in the body of the animal was readily available for conversion to serum proteins, but the bulk of the protein in the tissues resisted this contribution. The more readily available part of the protein tissue of the body was referred to as labile, or a “reserve.” This fraction could be called upon for restoration of the serum proteins without serious interference with the functioning of other protein tissues. It was not visualized as a pool of protein apart from organized tissues.

An outstanding aspect of study of body composition is the discovery that protein-containing tissues are regularly formed in a fixed fashion; the fat-free composition of the tissues becomes constant at chemical maturity and cannot be varied by diet. This fact denies the possibility of storing a significant amount of protein in a reserve apart from the tissues, which could be called upon for their maintenance when the daily intake of protein is insufficient. The formation of protein-containing tissues proceeds in a methodical fashion to utilize almost all the nitrogen that is retained in the body. Except for the materials in transit in the circulation and body fluids, the nitrogenous substances not accommodated in the fixed composition of the tissues must be eliminated in the excreta. When the daily intake of protein is inadequate to maintain the existing protein-containing tissues, the preservation of one tissue (e.g., plasma proteins) is at the expense of another—no uncommitted, unorganized reserve of nitrogenous material or protein of significance has been demonstrated.

“Fixed composition of the fat-free tissues” should not be interpreted to mean that there is not a level of dietary intake of protein which will be conducive to attainment of maximum size and an attendant maximum mass of protein incorporated in the tissues. There may be a state of nutrition in which a portion of various tissues can be converted to serve more pressing needs of other tissues, without detectable disturbances in the donor tissues or organs. It cannot be assumed that this phenomenon means that an excessive intake of protein can lead to greater “reserves” of protein in the individual or make him better prepared to withstand deprivation or “stress.” Conceivably the greater intake of protein required to maintain an existing larger
amount in the body could prove to be a handicap under adverse conditions.

This question of nutritional advantage or disadvantage to maximal deposition of protein in the tissues is extremely difficult to subject to controlled study in human populations. The available evidence does not suggest that, under modern conditions of infant feeding, any formula of cow's milk providing intakes of protein greater than that of breast-fed infants affords improvement in growth, increased resistance to disease, greater survival, better health or speedier recovery from illness.

Furthermore, if there is no significant storage of protein, apart from organized tissues, it follows that protein (amino acids) absorbed in excess of that which can be utilized in the formation and maintenance of the tissues of fixed percentage composition must either be eliminated from the body through degradation and excretion of the end-products, or metabolized to provide energy for immediate use, or be partially converted into carbohydrate or fat for storage in these compartments. The greater gains in animals receiving higher intakes of protein are largely accounted for by more fat in the tissues (Table III). It is unreasonable to force the organism to become obese or to satisfy its need for calories from protein by inclusion of an unnecessary percentage of protein in the diet with consequent reduction in the percentages of carbohydrate and fat.

Regardless of the requirement for formation of protein-containing tissues, the protein ingested is absorbed to the extent of 95% so that an excessive intake inevitably imposes a metabolic burden on the organism. Deleterious consequences of this under the conditions commonly employed in feeding of infants (when the higher intakes of protein are provided by cow's-milk formulae offering % of calories from the milk), other than the implications for water requirement, have not been detected. Although no immediate harm has been observed, it is conceivable that damage to the kidneys (not evident in infancy) might occur; experiments in rats reveal that pathologic lesions, ordinarily seen in the kidneys of aged rats, are made to appear at much earlier ages by as little as a twofold increase in the load of protein and corresponding increase in degradation products to be excreted.53

CONCLUDING COMMENTS

This essay is not intended to be a comprehensive treatment of the subject. A vast array of relevant material is not mentioned, not from willful neglect, but because it was not essential for the development of the theme although it may have provided convincing elaboration. Those familiar with the general subject will realize that other aspects have been adequately presented elsewhere.

Nor should the impression be gained that the limitations dwelt upon indicate a pessimistic or nihilistic attitude towards ultimate improvement in techniques for appraisal of nutritional status and in the means of achieving optimal nutrition.

It is hoped that the considerations presented will be given due weight in future attempts to set figures for dietary allowances of specific nutrients and that the proper significance of a proposed allowance may be more generally realized. As a result, the impact of some of the biased or unsupported suggestions which are used in promotion of particular infant foods may be lessened.

It appears that excessive preoccupation with size and composition of the body should not deter more active interest in the qualitative significance of nutrition—the development of means of appraising the functional performance engendered by different diets. Reconsideration of the goals of nutrition will stimulate the discovery of the techniques required to advance in the chosen direction. Otherwise stagnation and sterility will foreshadow decay in the science of nutrition.

A dietary allowance may be essentially an abstract notion, but it is unreasonable to disregard the wide variations in protein in-
take currently provided in infant feeding. The food intake is governed by caloric requirements: the percentage of calories provided as protein in human milk is 7%, while in the commonly employed formula of cow's milk (% of calories from the milk) protein furnishes 15% of the calories consumed, and products purported to resemble human milk offer about 11% of the calories as protein. If, under the guise of simplicity and generosity, the use of unmodified whole cow's milk should gain adherents, the unsuspecting infants will receive 22% of their caloric intake as protein!

It is easy to see that something more than the almost mystical concept of "reserves" to meet "stress" should be required to justify intakes of protein greatly in excess of that received by infants fed at the breast. The burden of proof has shifted onto the advocates of high intakes of protein; and the mere survival of hosts of infants over the years, unwarranted extrapolations from remotely relevant and limited studies of lower animals, and poorly designed and uncontrolled studies with infants must not be accepted as substantial arguments.

Likewise, the exact equivalence of the protein in human and cow's milk cannot be regarded as established, nor should the final selection of the correct artificial feeding for infants be based on the appealing jargon of teleologists.

A proper attitude to govern further efforts to find the appropriate nutrition to foster optimal performance is that expressed by Schneider in summing up a conference of workers grappling with a similar question—the relation of nutrition to infection:

...we are confronted with an ad hoc necessity of searching for evidence of the supposed connection between nutrition and infection. On such an occasion, plausibility is not enough; the construction of possible and labyrinthine connections is not enough; only proof will suffice.

There are ever-present threats to the freedom of the investigator: the inclination to defend a position that earned him his reputation long after reason insists upon a change in opinion; and the subtle machinations of those vested interests which seek to direct his investigations by selective support of research promising to benefit their cause. Academic investigators make their findings freely available; profits derived from the applications of research should be freely devoted to fundamental studies.

These threats may be opposed by objectivity in the investigator and alertness on the part of educators. It is their responsibility to maintain a dominant influence in practical nutrition by taking pains to present the fundamentals of nutrition so clearly that the practitioner will be prepared to withstand the distracting "educational" material often poured forth in the service of promotion.

This is not to deny the excellence in the technology of manufacturers, without whose aid the feeding of infants would never have progressed so satisfactorily. It seems fair to say that every group concerned may make a contribution, but the infants may be better served if one group does not usurp the prerogative of another.

It is inevitable that a lack of enterprise in the profession will open the way to inroad by some other group, and this is as it should be—the privilege to lead must be earned, not inherited.

REFERENCES


DETERRMINATION AND SIGNIFICANCE OF A DIETARY ALLOWANCE OF PROTEIN FOR INFANTS: Needed: A Shift of Emphasis in Nutrition
Charles D. May

*Pediatrics* 1959;23:384

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