The Institute of Biology's Studies in Biology no. 141

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General Preface to the Series

Because it is no longer possible for one textbook to cover the whole field of biology while remaining sufficiently up to date, the Institute of Biology proposed this series so that teachers and students can learn about significant developments. The enthusiastic acceptance of 'Studies in Biology' shows that the books are providing authoritative views of biological topics.

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Readers' comments will be welcomed by the Education Officer of the Institute.

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Preface

This book is a sequel to book no. 94 in this series, *Principles of Human Nutrition*. The earlier book was mainly concerned with theoretical aspects of nutrition whereas the present one is devoted to more practical matters and it assumes a knowledge of basic principles. Thus, for example, the concept of protein quality is not defined and it is assumed that the reader knows what fats, carbohydrates, minerals and vitamins are. Only in this way was it possible to maximize the amount of new material that could be included.

The central theme of the book is 'Nutrition and Health' and the aim throughout is to give an up to date account of this relationship and, on the other side of the coin, of the relationship between nutrition and some important disease conditions. All too many nutritionists in their popular writings attribute excessive importance to individual nutrients such as sugar, fat or fibre, for example, thereby confusing the public and ignoring the first principle of nutrition which is that all nutrients are important and all must be balanced with respect to one another. This book attempts to present a balanced view of particular areas of nutrition, selected on the basis of their importance to health.

Southampton, 1982 T. G. T.

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1 General Aspects of Nutrition and Health

1.1 Introduction

The link between nutrition and health is generally accepted and this link is most clearly demonstrable in cases of extreme under- or over-nutrition, examples of which are considered in Chapters 2 and 3 respectively. The term *malnutrition* embraces both under- and over-nutrition and there is a range of intake of individual nutrients and of energy in between these two extreme situations, narrow for some nutrients, wider for others, which promotes a state of optimum nutrition. The concept of optimum *ranges* of intake is important and it carries the implication that the body is able to compensate for slight excesses and deficiencies of most nutrients. (Compensation for excessive and deficient intakes of energy is less straightforward: see pp. 26–8 and 10–11, respectively.)

It is also possible to recognize sub-optimal states of nutrition, particularly with respect to deficiencies of vitamins, that are not sufficiently severe to classify as malnutrition. These marginal deficiency states are probably responsible for more ill-health in industrial societies than conditions of overt under-nutrition and deficiencies of several vitamins may occur together in the same individual. Marginal or sub-clinical nutritional deficiencies are by their very nature difficult to identify with any degree of certainty, since they do not present themselves in the form of well defined clinical signs or symptoms but they are real nevertheless. The symptoms are, in fact, quite non-specific and they vary with the individual and with the particular deficiency: tiredness, lassitude, depression, apathy, irritability and a general malaise are among the commonest ones observed and the same symptoms may occur in well nourished individuals for reasons quite unrelated to nutrition.

'Marginal nutritional excesses' do not constitute a problem since intakes of protein, vitamins and minerals two or three times physiological requirements do not result in any untoward effects. Intakes of quite small excesses of energy over and above requirements may, however, induce obesity in the long term.

1.2 Physiological requirements and recommended intakes (or allowances)

Every individual has a physiological requirement for each nutrient, i.e. the minimum amount of each which will maintain health in adults and permit normal growth in children. These requirements naturally vary according to age, sex and body weight but, in addition, there are considerable variations in requirements between individuals who in other respects are very similar. Thus, requirements should, ideally, be expressed in terms of a mean and standard deviation (SD) in order to quantify the extent of this variation. If, for example, the requirement of an adult man for a particular nutrient is expressed as 20 ± 2 mg day^{-1}, this means that 95% of all such men have a requirement within the range 16–24 mg day^{-1}, i.e. two SDs on either side of the mean and that 2.5% have a requirement below and 2.5% a requirement above this range (Fig. 1-1), assuming a normal distribution. Recommended daily intakes (RDIs) apply to populations and they are based on mean physiological requirements plus 2SDs plus appropriate 'safety margins'.

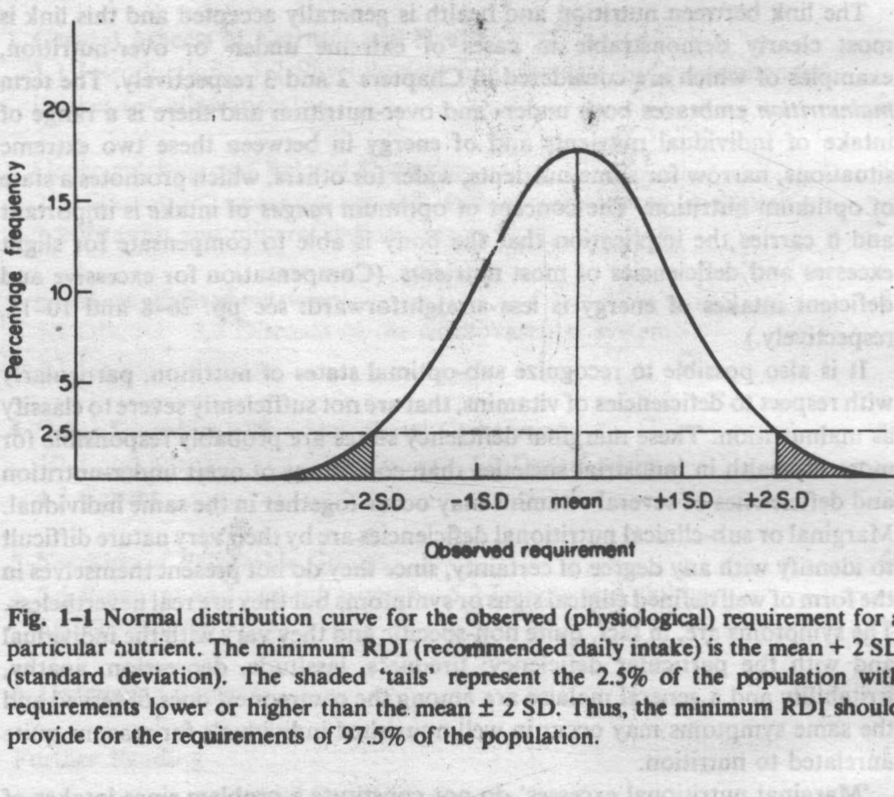

Fig. 1-1 Normal distribution curve for the observed (physiological) requirement for a particular nutrient. The minimum RDI (recommended daily intake) is the mean + 2 SD (standard deviation). The shaded 'tails' represent the 2.5% of the population with requirements lower or higher than the mean ± 2 SD. Thus, the minimum RDI should provide for the requirements of 97.5% of the population.

Many countries and the World Health Organization (WHO) and Food and Agriculture Organization (FAO) of the United Nations have published tables giving RDIs for all the most important nutrients for males and females according to age and in relation to pregnancy and lactation. RDIs are mainly used for planning purposes, e.g. in planning diets and food purchases for institutions such as schools, orphanages and mental hospitals and for expeditions, and for assessing the adequacy of the nutrient intake of populations whose food consumption has been estimated from dietary surveys, thus enabling groups with low intakes of particular nutrients to be identified. International agencies require to know how much food is needed for famine relief and for other programmes, and national governments need to calculate food supplies for their populations in relation to agricultural production and to food imports. In order to make the necessary calculations the average RDIs for the populations in question, based on their age and sex distribution, must be known.

A more recent use of RDIs, different in nature from the foregoing uses, is in relation to the 'nutritional labelling' of canned and packaged foods, which bear labels giving the proportion of the RDI of the most important nutrients provided by the contents of the pack or by a normal serving of it. Different criteria are used for establishing RDIs for the different nutrients and for energy.

Vitamins The first step in determining RDIs for vitamins is to establish by experiment the minimum daily intake that will prevent the characteristic clinical signs and symptoms of deficiency from developing or cure these signs and symptoms once they have appeared. This often means that volunteers consume a diet grossly deficient in the vitamin under test, but adequate in all other respects, until signs of a deficiency appear. The minimum amount of the vitamin needed to cure the deficiency is then determined by giving graded doses of the pure vitamin. The resulting mean values ± SDs represent the starting points from which physiological requirements and RDIs evolve but it is clear from the previous discussion of conditions of marginal deficiency that the mere absence of clinical signs and symptoms is unlikely to indicate optimum nutrition. Additions have, therefore, to be made to these minima to provide a margin of safety against sub-clinical deficiencies and to ensure that the tissues have sufficient reserves of the vitamins to cover day to day fluctuations in intake and to provide for possible increases in requirement due to the stress and strains of everyday life. There is no general formula for deciding just how large these safety factors, different for different vitamins, should be, and traditionally it has been left to committees of experts to make recommendations on the basis of their combined wisdom and experience.

Recommendations for some of the less important vitamins, e.g. biotin and pantothenic acid, have not been determined with any degree of precision.

Minerals The only minerals that figure in British tables of RDI are calcium and iron but magnesium, iodine and zinc are sometimes included in tables published in other countries. Requirements for calcium, phosphorus and magnesium are determined using the 'balance' techniques, i.e. by determining the minimum dietary supply that will ensure that losses from the body in urine and faeces equal the amount provided in the food. More balances have been carried out for calcium than for any other mineral because of the importance of this element in the normal growth and development of the skeleton and in various metabolic diseases of bone. Requirements for iron are based on the minimum amounts needed to maintain normal levels of haemoglobin in the blood and those for iodine on the amounts needed to prevent the development of goitre. In the case of iron, dietary requirements vary according to the nature of the diet: the iron present in plant materials is substantially less available than the iron of animal foods and the iron requirements of people consuming few or no foods of animal origin may be twice as high as those of people consuming a mixed diet.

As in the case of vitamins, in order to produce RDIs, additions have to be made to these minimum requirements to cater both for the needs of those with above average requirements and to provide a margin of safety.

Protein The most satisfactory method for assessing protein requirements is by determining (by means of balance experiments) the lowest protein intake that will permit nitrogen equilibrium in adults and satisfactory growth and nitrogen retention in children. (On average, proteins contain 16% nitrogen and it is possible, therefore, to interconvert values for protein and nitrogen using this percentage.) A joint FAO/WHO *ad hoc* expert committee issued a report on Energy and Protein Requirements in 1973 in which the results of a number of such studies were collected together and the average nitrogen intake required to maintain balance in 75 subjects of both sexes, allowing a small amount of losses through the skin and for other minor losses, was 77 mg N per kg body weight per day when the dietary protein consisted of milk, egg, casein or a mixture of proteins including some of animal origin. The corresponding value when mixtures of plant protein were consumed was 93 mg N but when single sources of poor-quality plant proteins were consumed, a somewhat unrealistic situation except in the short term, the minimum requirement was up to 25% higher than this value.

Another method of estimating minimum requirements for protein is the 'factorial' method, whereby the minimum obligatory losses of nitrogen in the urine and faeces and through the skin when a nitrogen-free diet is consumed are totalled. For children this total is increased by the amount stored during growth, and for pregnant women by the amount stored in the foetus, foetal membranes and maternal tissue at the different stages of pregnancy. For lactating women, the amount of protein secreted in the milk must also be provided for.

When the minimum nitrogen requirements calculated by the factorial method are compared with the values obtained by the balance technique, the latter values are found to be about one-third higher than the former. This is not surprising, since it is known that dietary protein is not used with 100% efficiency by man: even when high quality proteins such as milk and eggs are given the efficiency with which their nitrogen is used is only about 70%. Thus, for example, an individual whose obligatory losses of nitrogen on a protein-free diet is 5 g would need approximately $5 \times 100/70 = 7.1$ g nitrogen, i.e. $7.1 \times 6.25 = 44$g protein of high quality per day to maintain nitrogen balance.

Table 1 summarizes the recommendations of the joint FAO/WHO expert committee and is reproduced by kind permission of the FAO. In the Table the calculated values for nitrogen requirements are averages and to derive RDIs or 'safe levels of intake' to use the expression favoured by the committee, these average values are increased by 30%, twice the coefficient of variation of 15% found in the nitrogen balance experiments, to ensure that the need of most of those individuals with the highest requirements are met. (The coefficient of variation is the standard deviation (SD) expressed as a percentage of the mean, i.e. (SD/mean) $\times$ 100.) It should be noted that these 'safe levels of intake' are for nitrogen in the form of a high quality protein such as milk or egg or a mixture of proteins equally high in quality. When proteins of inferior quality are consumed, larger amounts are needed to achieve nitrogen balance. The actual adjustment is based either on the protein score or on the net protein utilization (NPU) of the protein. Both these measures of protein quality derive numerical values for food proteins relative to egg or milk and the safe level of intake of any food protein is determined by the relationship:

$$\frac{\text{NPU (or chemical score) of egg or milk}}{\text{NPU of food protein}} \times \text{safe level of intake of egg or milk}$$

In 1975, the Committee on International Dietary Allowances of the International Union of Nutritional Sciences published a survey of recommended nutrient intakes in different countries. Protein allowances for young adult men varied from 53 to 85 g day^{-1} based on an NPU of 70. These differences reflect in

Table 1 Safe levels of intake of egg or milk protein.

Age	*Total nitrogen requirements – obligatory losses and growth* (mg nitrogen kg^{-1} day^{-1})		*Adjusted nitrogen requirements – increased by 30% in accordance with balance and growth data* (mg nitrogen kg^{-1} day^{-1})		*Safe level of intake (adjusted requirement + 30% to allow for individual variability)* (mg nitrogen kg^{-1} day^{-1})		(g protein kg^{-1} day^{-1})	
(Months)								
<3					384a		2.40[a]	
3–5					296a		1.85[a]	
6–9	154		200		260		1.62	
9–11	136		177		230		1.44	
(Years)								
1	120		156		203		1.27	
2	112		146		190		1.19	
3	106		138		179		1.12	
4	100		130		169		1.06	
5	96		125		162		1.01	
6	92		120		156		0.98	
7	88		114		148		0.92	
8	83		108		140		0.87	
9	80		104		135		0.85	
	M	F	M	F	M	F	M	F
10	78	77	101	100	132	130	0.82	0.81
11	77	72	100	94	130	122	0.81	0.76
12	74	70	96	91	125	118	0.78	0.74
13	73	64	95	83	123	108	0.77	0.68
14	68	59	88	77	115	100	0.72	0.62
15	63	56	82	73	107	95	0.67	0.59
16	61	55	79	71	103	93	0.64	0.58
17	58	54	75	70	98	91	0.61	0.57
Adult	54	49	70	64	91	83	0.57	0.52

a Based on observed intakes (mean + 2 standard deviations) of healthy infants. M, males; F, females.

some measure the availability of foods in the different countries and, in general, recommendations are higher for affluent countries than for developing ones. In Britain, a report from the Department of Health and Social Security (DHSS) recommends a daily protein intake based on 10% of the energy intake and this gives an RDI for an adult man of 68 g. However, the DHSS report gives a *minimum* requirement of 45 g protein for men.

It is interesting to compare the safe level of protein intake recommended by the joint FAO/WHO committee, which is the lowest recommendation of any official body, with the intake of breast-fed infants, whose requirements are greater than at any other time of life. Breast milk contains 6–7% of its energy as protein and the 'safe level' of high quality protein recommended for adults by the FAO/WHO Committee works out to be 5–5.5% of the energy intake. This 'safe level' of protein intake is best regarded as equivalent to the upper limit of the normal range of physiological requirements and it is consistent with, i.e. somewhat less than, the 'natural intake' of breast-fed infants in relation to their energy intake. The RDIs of most countries are about twice physiological requirements to provide a margin of safety and to take account of the fact that the quality of the dietary protein is likely to be significantly less than that of egg or milk. Adjustments for protein quality are more important for children and pregnant and nursing women than for adult men and other women and there is some evidence that adult humans utilize essential amino acids more efficiently than rats when consuming sufficient protein to maintain nitrogen balance. It seems probable that some, perhaps all, of the essential amino acids are recycled to a greater extent in adult men and women than in the young growing rats that are used for NPU determinations and it may simply be that essential amino acids are used more efficiently for maintenance than for growth, rather than that there is a species difference between rats and men.

It must be emphasized that, in the words of the FAO/WHO committee on energy and protein requirements 'All estimates of protein requirements are valid only when energy requirements are fully met. When the total energy intake is inadequate, some dietary protein is used for energy and is not available to satisfy protein needs'.

Energy Estimates of requirements for energy differ from those for other components of the diet in that no additions have to be made to provide a margin of safety and they are complicated by the fact that energy requirements vary according to climate, in particular to temperature, and to the physical activity of the individual and, therefore, of populations. A peasant population, engaged in hard manual work, clearly has a higher requirement for energy than a population of the same age and sex distribution engaged mainly in office work. Tables of energy requirements, therefore, take account of physical activity. Having said this, however, it must be stated that variations in energy requirements between individuals of the same age, sex, weight and physical activity are very great.

The extent of this variation is shown in Fig. 1–2 for adults and Fig. 1–3 for children. In both sexes some individuals of any particular age habitually consume twice as much energy per day as others and some one-year-old children eat more than some adults. Differences in basal metabolism, in physical activity

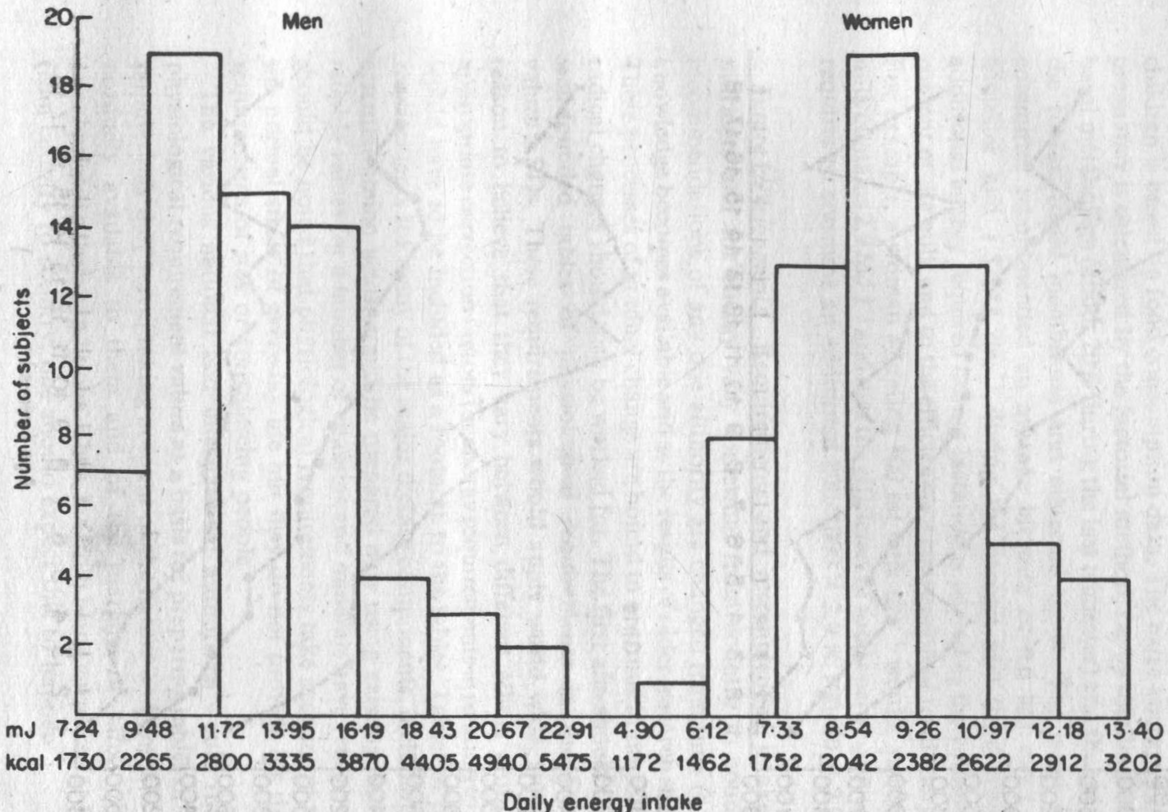

Fig. 1–2 Histogram showing the frequency distribution of daily energy intake of 63 men and 63 women (based on Fig. 1 of the paper 'Individual Variation' by E.M. Widdowson in Proceedings of the Nutrition Society, vol. *21* (1962) p. 122 and published by Cambridge University Press: reproduced by permission of the author and publisher).

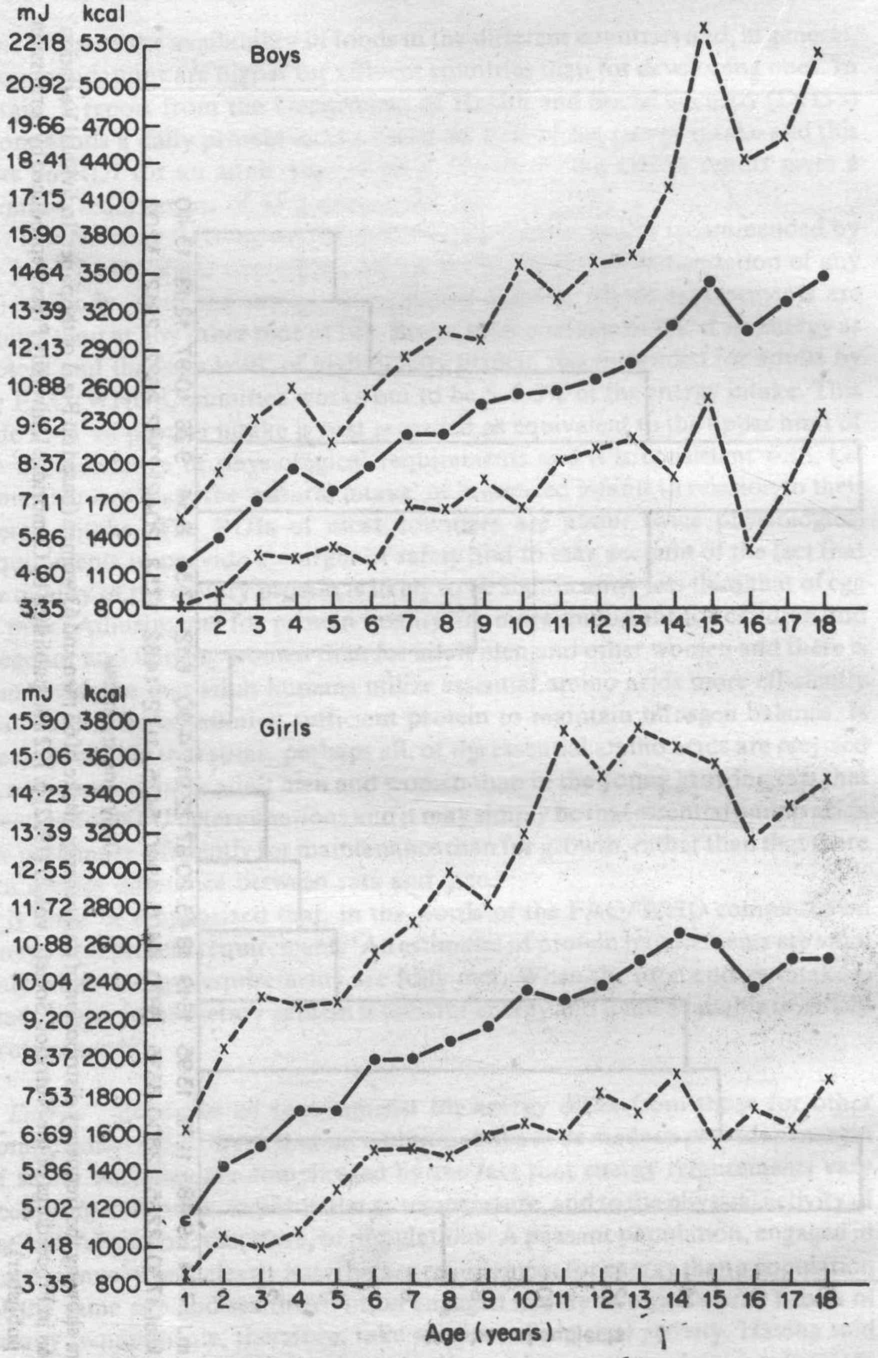

Fig. 1–3 Mean daily energy intake for boys and girls in relation to age (●) mean values for at least twenty at each age. Maximum and minimum intakes are also shown (X). (Values are taken from the Medical Research Council Special Report Series No.257 (1947) by E.M. Widdowson and published by permission of the Controller of Her Majesty's Stationery Office.)

and in the thermic effect of feeding (see pp. 26–7) are known to contribute to this variability and there may well be additional factors, but body weight is of minor importance.

Energy requirements may be assessed by measuring either food intake or energy expenditure and for individuals who are neither gaining nor losing weight the result should be the same by the two methods. The energy required by children is based on food consumption data. The extra energy required during pregnancy is calculated by the factorial method, i.e. by totalling the increase in basal metabolism (about 20% during the last trimester) and the energy stored in the foetus, foetal membranes and maternal tissue. The latest FAO/WHO committee recommended an average increase of 0.6 MJ day^{-1} in the first trimester and 1.5 MJ day^{-1} during the second and third trimesters. The additional energy required during lactation is related to the volume and energy content of the milk and to the efficiency of conversion of food energy into milk. For example, a woman secreting 800 ml milk day^{-1} would, assuming that the milk contains 2.9 MJ l^{-1} and that the efficiency of food energy conversion is 80%, requires to consume an additional $800/1000 \times 2.9 \times 100/80 = 2.9$ MJ day^{-1}.

Future developments Requirements and recommended intakes for many nutrients and for energy vary somewhat from country to country and the recommendations of any one authority are changed from time to time as new knowledge becomes available and as the results of older research are re-assessed. These processes of gradual change are bound to continue in the future but more radical changes should also be worked for. The first aim should be to establish well-founded tables of physiological requirements in the form of mean values ± SDs. These requirements would apply world wide, since there is no reason to believe that they vary between different ethnic groups, although appropriate correction factors for energy requirements in relation to temperature would have to be included as a footnote to the tables. Tables of physiological requirements for many of the major dietary components, including some of the essential amino acids, could be prepared now using existing information but reliable values for a number of vitamins and minerals have yet to be obtained. It should be noted that physiological requirements take account of the effects of the normal stress of everyday life but they do not provide for the additional requirements of sick or convalescing people.

The various national and international authorities would then use these physiological requirement values as a basis for preparing tables of RDIs for the populations they serve, taking account of the nature and amount of the foods normally available to them and of the margins of safety they consider appropriate to their conditions. Thus, far from being surprised at RDIs varying from country to country, one should expect this to happen.

2 Under-Nutrition and Related Conditions

2.1 Starvation, *anorexia nervosa* and protein-energy malnutrition

Starvation This is the most extreme form of under-nutrition: traditionally, one associates it with famine caused by natural disasters such as drought, floods or pestilence and with concentration camps, but starvation, partial or total, can also occur in circumstances nearer home, as for example in hunger strikes, in untreated coeliac disease (p. 41), *anorexia nervosa*, and *dysphagia* (in which patients have difficulty in swallowing).

Most healthy adults can lose 25% of their body weight as a result of starvation without suffering permanent damage. Table 2 shows the effect of this degree of starvation on body composition. Obese people can lose more than 25%, but danger to life increases progressively as loss of body weight increases beyond this limit.

Table 2 Changes in the body composition of an average man after losing 25% of his body weight due to starvation.

	Normal (kg)	*After starvation* (kg)	*% loss*
Protein	11.5	8.5	26
Fat	9.0	2.5	72
Carbohydrate	0.5	0.3	40
Water			
Extracellular	15.0	15.0	0
Intracellular	25.0	19.0	24
Minerals	4.0	3.5	12
Total body weight	65	48.8	25

Tissue wasting and weight loss are rapid in the initial stages of starvation but the rate of loss gradually slows down as adaptive changes, evolved presumably in response to early man's exposure to intermittent food supplies, come into play. In the first few days of starvation, 1.5–2 kg of weight may be lost, due mainly to losses of glycogen, protein and water and the same phenomenon is observed in the early stages of dieting (p. 29). During the first week of starvation, nitrogen excretion in the urine falls from perhaps 12 g d^{-1} (equivalent to 75 g protein) to 6 g d^{-1} after 3 d, reaching a minimum of about 4.7 g d^{-1} after several weeks of starvation. The adaptive changes serve to conserve body protein, to provide the minimum glucose for essential metabolic purposes (e.g. for the red cells and the brain) and to utilize fat stores to the maximum extent. The brain normally uses glucose as an energy source but in starvation ketone bodies (derived from fat) replace glucose to an increasing extent.

It is not possible to adapt fully to complete starvation but adaptation to semi-starvation can be virtually complete. In the well-known 'Minnesota experiment' 32 men spent six weeks on mean energy intakes less than half of normal (6.57 compared with 14.62 MJ d^{-1}) and at the end of this time they had almost regained energy balance at their new reduced body weight by reducing basal metabolism and physical activity: the thermic effect of feeding (pp. 26–7) was also lower.

Prolonged starvation is characterized by extreme muscle wasting, a loose dry skin, oedema and low pulse rate and blood pressure. Severe personality changes may occur and the mind becomes wholly obsessed with thoughts of food. The rehabilitation of starving people is not difficult provided that atrophy of, and degenerative changes in, the organs and systems of the body have not progressed too far: all they need is food. In cases of extreme and prolonged starvation, however, rehabilitation can be hazardous and even fatal unless extreme care is exercised. In this condition, the smooth muscles, the glands and the mucosa (the layer of absorptive cells) of the intestines atrophy and the walls become almost paper-thin. If the powers of digestion and absorption are completely lost, death is inevitable, but if some digestive function remains there is hope of recovery. Bland, highly digestible foods should be given in very small meals, particularly if there is diarrhoea. Cooked baby cereal made up with skimmed milk and given in the form of a thin porridge is ideal but not always available. Once the victim is taking food well, increasing amounts should be given to satisfy the appetite.

Anorexia nervosa This is a disease of psychiatric origin in which the patient refuses to eat. It can be fatal. It occurs most frequently in adolescent girls and young women between the ages of 15 and 25 but it can also occur in older women and in men. Once a very rare condition, its prevalence seems to have increased in recent years, mainly among the middle-classes. Its essential feature is an obsessional wish to avoid any suspicion of plumpness and it has been called the 'slimmer's disease', because it often develops from a normal desire to slim by dieting. Patients exhibit a completely distorted view of their bodily conformation: whereas they are, in fact, extremely thin and emaciated, they insist that they are fat. It is as though they are permanently looking at themselves in a distorting mirror located in their mind's eye. The medical and psychological histories of patients show few common features but many are anxious and insecure, possibly as a result of family conflicts. They are depressed, and many have psycho-sexual problems. In true anorexia the patients lose all desire to eat and in the initial stages of their rehabilitation intravenous feeding may have to be resorted to. There is another psychiatric condition, similar in some respects to anorexia, in which patients have continually to repress the desire to eat. Sometimes, they give way to this desire and engage in huge binges, after which they may deliberately vomit the contents of their stomachs or purge themselves repeatedly.

In treating anorexia nervosa, the basic problem, of course, is to get the patient to eat. Since anorexia nervosa is a psychiatric disease, successful treatment must include a psychiatric component. If the condition is not to recur once normal weight has been regained as a result of hospital treatment, the patient needs continuous support and understanding from family and friends and the help of the psychiatric social worker.

Protein energy-malnutrition In a global context, protein-energy malnutrition (PEM) in children in third-world countries is the most serious nutritional disease of all, both quantitatively, in terms of the vast numbers involved, and qualitatively, in terms of the human misery it encompasses. In some under-developed countries, one-third of all children born die before reaching the age of five either from PEM itself or from the diseases that accompany it. The term PEM covers a wide spectrum of clinical conditions: the two extremes are *marasmus* and *kwashiorkor* and there are various intermediate conditions between these extremes. Before discussing the detailed clinical features of these conditions, a brief consideration of normal growth in children is appropriate.

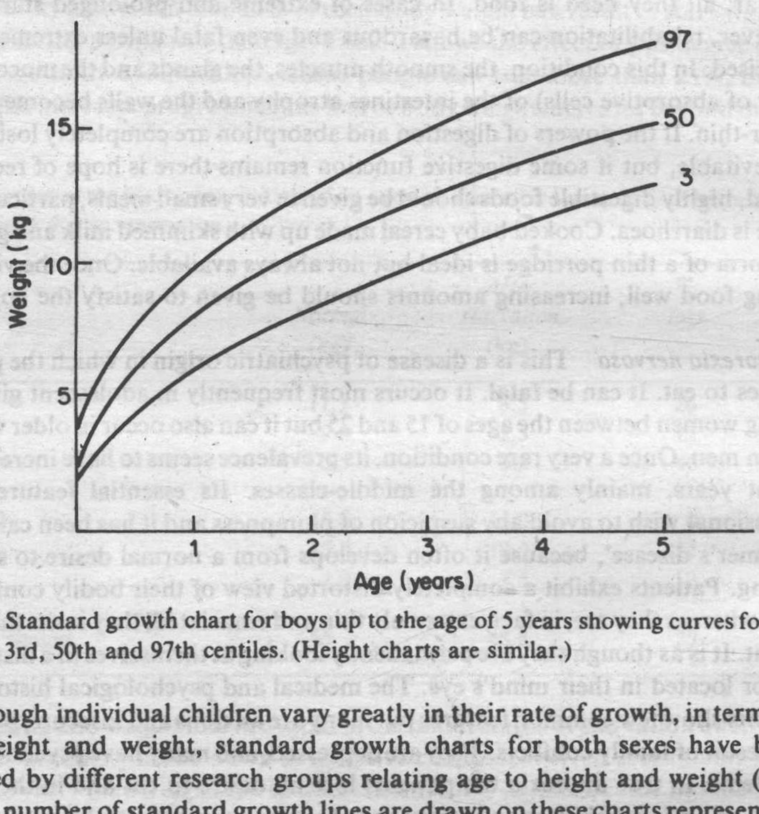

Fig. 2–1 Standard growth chart for boys up to the age of 5 years showing curves for the 3rd, 50th and 97th centiles. (Height charts are similar.)

Although individual children vary greatly in their rate of growth, in terms of both height and weight, standard growth charts for both sexes have been prepared by different research groups relating age to height and weight (Fig. 2–1). A number of standard growth lines are drawn on these charts representing 'high', 'low' and 'medium' rates of growth. The last, the so-called 50th percentile line represents the median growth line, while the 3rd and 97th percentiles represent the lines for the 3% of the population with, respectively, the lowest and highest rates of growth. The growth curve of a normal child runs parallel to the percentile lines but when growth falters and the curve falls below the percentile line on which it started this constitutes a danger signal that PEM is imminent.

Kwashiorkor occurs mainly in older infants and young children who have