

ample demonstration that sanitation and the establishment of a reliable, good-quality water supply were the decisive factors in eliminating many of the major infectious diseases which were no less threatening to Europe a century or two ago than parasitic diseases still are to many parts of our world today.

Within the multifaceted context of parasitic disease, molecular biology and its scientific ramifications have contributed significantly, and will continue to do so, both to our understanding of basic mechanisms of parasite biology and its interaction with that of hosts and vectors, and to the development of novel and more efficient diagnostic and, it is to be hoped, therapeutic tools. Nevertheless, it would certainly be unwise to expect a solution for every problem to be found in the pills and potions eventually developed by recombinant DNA technology, and it will be helpful for all involved to keep the perspective right by remembering the profound insight of the great parasitologist William Trager: 'Good plumbing has done more for good health than has good medicine'.

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## Unsolved and controversial issues in human nutrition

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### Unsolved and controversial issues in human nutrition. Introduction

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There are particular areas in medical research where our knowledge is growing rapidly and where certain concepts are constantly being challenged and questioned. Research in human nutrition is a potential candidate for controversy owing to a number of limitations related to experimental, ethical, statistical, environmental and genetic considerations. Indeed, in the field of nutrition and health pseudo-scientific beliefs, speculations based on emotional discussion rather than experimental evidence,

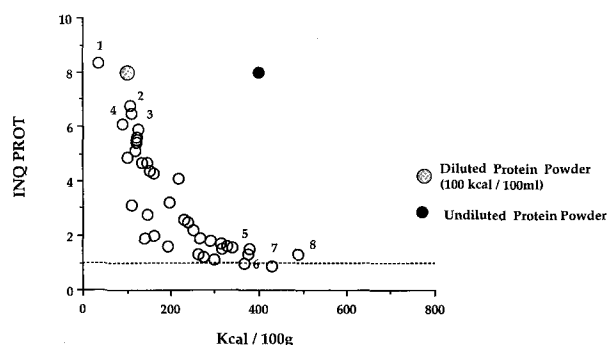
and dogmatic positions (i.e. food faddism and quackery) appear still to be widely prevalent. For example, the belief that megadoses of certain nutrients (in particular a number of vitamins and several trace elements) have unique preventive or curative properties in man may be more widely disseminated than currently thought.

The Swiss Nutrition Society organizes a symposium every 3 years dealing with a topic where new information has been generated and updated information is required.

The present topic makes a break with more conventional themes selected in the two previous symposia which dealt with 'Digestion and absorption of nutrients' (1983) and 'Control of food intake in man' (1986). The information collected in this review covers certain nutritional issues such as the physiological and nutritional importance of polyunsaturated fatty acids, dietary fibres, and selenium in man. Other reports deal with the effects of a supra-physiological intake of vitamins or amino acids or proteins in man. The selection of these topics was somewhat arbitrary, since it is evident that many other areas of nutritional research also merit further up-to-date examination.

The present attempts to put together such apparently heterogeneous nutritional topics in one review is in itself a challenging task. It should be kept in mind, however, that human beings eat food and not isolated nutrients, and that food must satisfy the requirement for energy (the largest nutritional component of the diet – if one excepts  $H_2O$ ), proteins (the second largest component of nutrient requirements), essential fatty acids, minerals, vitamins and trace elements. Complex interactions between macronutrients and micronutrients occur in intermediary metabolism. For example, interaction of energy and vitamins is evidenced by the fact that some water-soluble vitamins serve as cofactors in oxidative reactions, like thiamin (vitamin  $B_1$ ), which is a coenzyme in various reactions of carbohydrate metabolism. Therefore, the amount of dietary energy sources, in particular carbohydrates, may modify the energy needs of the body tissues and influence the requirement for vitamins. This explains why recommended dietary allowances currently express the requirement for some water-soluble vitamins such as thiamin, riboflavin and niacin in relation to the total energy intake, i.e. in mg/1000 kcal.

In this introduction it is worth emphasizing the relatively new concept of 'nutrient density of food' which is of great importance for the assessment of the nutritional quality of a diet and which has not been highlighted in the papers presented. Food needs to satisfy not only the total energy requirement but also the requirement for other nutrients, so that the concentration of a given nutrient relative to energy is a useful way of expressing the intake of that nutrient. The nutrient density is calculated as follows: 1) the concentration of a given nutrient in a food is expressed as a function of its metabolizable energy (for example for protein, in grams per 1000 kcal), 2) the nutrient allowances for a given age group and sex are calculated in the same units, using the recommended dietary allowances. In human nutrition, the ratio of the former divided by the latter has been called the 'index of nutritional quality', abbreviated INQ<sup>2</sup>. It represents the fraction of the nutrient requirement supplied by a given quantity of food relative to the fraction of energy requirement supplied by that quantity of food. This index can be calculated for each nutrient. For example, values for proteins of 1.0 and 2.0 indicate that the concentration



The index of nutritional quality (INQ) for protein is plotted against the energy density (expressed in kcal/g) for various foods. The dotted horizontal line represents an INQ = 1.0, corresponding to the recommended dietary allowances for an average adult man. 1 = Egg white; 2 = Turkey meat; 3 = Veal filet; 4 = Kidney; 5 = Lamb (shoulder); 6 = Lamb (chops); 7 = Duck; 8 = Salami.

of this nutrient in the diet, given at a level corresponding to the energy requirement, can fulfill 100% and 200% respectively of the protein allowances.

In addition to the nutrient density concept, the energy density of food is also an important characteristic of a diet, since a diet which is bulky (rich in dietary fibres) and of low energy density (poor in fat) will require the eating of a high food volume. In a growing child with a high relative energy requirement, this may hinder the satisfaction of energy requirements. In contrast, in an obese adult who is attempting to control food intake better in order to maintain energy equilibrium, a low energy-density diet rich in bulk may be helpful, since the control of food intake appears to be better achieved with meals of low rather than high energy density<sup>1,3</sup>. Therefore, in certain circumstances, a diet which combines a high nutrient density with a low energy density may be desirable in order to optimize the intake of various nutrients and to minimize the energy intake. The figure shows a graphical representation where both the nutrient density (in terms of proteins) and the energy density of various pre-selected foods can be visualized simultaneously. Such charts have recently been developed for a number of other nutrients (vitamins, minerals and trace elements) and are aimed at making it easier to select which food can be used to correct a potential deficiency or an excess of a given nutrient with regard to its energy content (Schutz and Baudat, unpublished results). From the figure, it can also be seen that one can select food with a high protein concentration (up to a factor from 6 to 8 times the protein allowances) and a low energy concentration (food on the top left of the diagram) or the reverse (foods on the bottom right of the diagram). The figure clearly indicates that it is possible to increase the amount of protein in the diet to supra-physiological levels by consuming specific foods without relying on pure protein supplementations. The concept also emphasizes that supplementation of a pure nutrient in the diet is not neces-

sarily a prerequisite for obtaining a large supply of that nutrient.

In public health and preventive medicine, emphasis is at present laid on the use of dietary modifications (and interventions) for controlling the chronic (non-communicable) and degenerative diseases that lead to high morbidity and mortality. Dietary guidelines for disease prevention have been set out by various international expert committees emphasizing which nutrients should be increased in the diet (for example complex carbohydrates, dietary fibres and some minerals) or reduced (total fats and saturated fats) as compared to current intakes. It should be realized that in spite of the large amount of work in progress in the nutrition field there are numerous

important questions which still deserve further investigation. The various papers presented here should not only provide updated information but also stimulate further research on both the basic and the applied aspects of nutritional science.

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## Effects of exaggerated amino acid and protein supply in man

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**Summary.** A general update review of the dynamic aspect of protein metabolism is presented. The effect of excess protein level on protein metabolism has been the object of a limited number of studies in man. From the information available, it appears that the primary regulatory pathway for body protein homeostasis is the process of amino acid (protein) oxidation.

**Key words.** Protein synthesis; protein breakdown; protein turnover; N balance; protein overfeeding; strength training; body composition.

### Introduction

The present day understanding of protein metabolism stems from Rudolf Schoenheimer's pioneering work with stable isotopes during the 1930s. A summary of most of these investigations can be found in a commemorative book which was published in 1942, shortly after his death<sup>12</sup>. In a series of studies in rats, Schoenheimer and his colleagues demonstrated two very important aspects of protein metabolism. The first was that amino acids from the diet, once absorbed, were kinetically indistinguishable from those already present in the body. This implied, therefore, that all amino acids, irrespective of whether they originated from the diet or from endogenous protein, could be considered kinetically as a single homogeneous metabolic pool within the body – a finding that was in direct opposition to the accepted opinion held at the time. The second and equally important observation was that the proteins which make up the body of the adult animal are not metabolically inert but are in a continuous state of being broken down into free amino acids and subsequently reincorporated back into protein. Although the concept of 'protein turnover' was actually first considered by Borsook and Kieghley, in 1935<sup>1</sup>, it was Schoenheimer and his associates<sup>12</sup> who provided the

firm experimental evidence to support its existence. This concept was also contrary to the generally accepted view held at that time which, except in the case of normal growth and tissue repair, regarded body protein as being metabolically inert. These two aspects, studied some fifty years ago in rats, form the basis of our present understanding of human protein metabolism – as outlined in figure 1 – and are important for appreciating the effects of changing dietary amino acid or protein supply. Schoenheimer's studies<sup>12</sup> generated a great deal of research interest in protein metabolism, especially in the influence that the composition of the diet had on it. The greater part of the work done subsequently, however, concentrated either on developing methods for assessing rates of protein synthesis and breakdown (turnover) or on the effects of protein and energy deficiencies on these processes (for reviews see Reeds and Garlick<sup>10</sup>, and Waterlow<sup>15</sup>). In contrast, very little work has been done on the consequences of an excessive dietary intake of amino acids and protein.

This account will cover the main features of whole-body amino acid and protein metabolism and will also describe a study in which the rate of protein turnover was measured in subjects consuming either normal or relatively high amounts of dietary protein.