

**Artificial feeds for the young infant : report / of the Working Party on the Composition of Foods for Infants and Young Children, Committee on Medical Aspects of Food Policy.**

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Department of Health and Social Security

Report on Health and Social Subjects

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# ARTIFICIAL FEEDS FOR THE YOUNG INFANT

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Report of the Working Party on the Composition of Foods for  
Infants and Young Children, Committee on Medical  
Aspects of Food Policy

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London



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# Committee on Medical Aspects of Food Policy

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## Preface

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The medical and nursing professions are convinced that when a mother can produce enough milk and wants to breast-feed her infant she should do so but for those mothers who do not breast-feed, artificial feeding will be necessary and alternatives to human milk must be available. Scientific knowledge has progressed rapidly in the past fifty years and suitable foods have been manufactured and marketed for some time.

More recently, knowledge of the composition of human milk has also increased and is still increasing. It is clear that no exact substitute for human milk is as yet possible. This is partly because the composition of human milk varies from one individual to another, and in one individual from one feed to another, and also because the species-specific immunological properties of human milk are difficult to imitate.

In 1974 it was announced that the Food Standards Committee would review foods for young infants in order to establish whether or not there is a need for standards or for other controls on the composition and description of such foods. This report is expected to be published shortly. When asked for advice about the nutritional aspects of the review, the Committee on Medical Aspects of Food Policy set up a Working Party of experts, under the Chairmanship of Professor T. E. Oppé, the members of which were both medically and scientifically qualified in the field of paediatric nutrition. The Working Party first made a study of the composition of mature human milk by modern analytical techniques. This was published in 1977<sup>1</sup>. The present report gives the full results of the Working Party's deliberations concerning guidelines for the nutrient composition of foods to be used when human milk is not available. Guidelines have been set in preference to a standard. This is because present knowledge is insufficiently advanced for exact recommendations to be made in relation to every component of a food. The guidelines also permit some of the variability in composition which is seen in human milk and which is necessary for the development of new products as further advances in knowledge are achieved.

These foods are the sole source of nourishment in the early months of life. The Working Party suggests that all new foods for young infants should be subject to scrutiny before being marketed in the United Kingdom so that mothers and those responsible for the feeding of young infants can be assured that such foods may be used with confidence. Present legislation is such that only certain of these foods, and then only with regard to certain constituents, are scrutinised by the Committee on Medical Aspects of Food Policy.

<sup>1</sup>Department of Health and Social Security, 1977. The composition of mature human milk. Report on Health and Social Subjects, No. 12. London, HMSO.

The Department is grateful to the members of both the Committee on Medical Aspects of Food Policy and to Professor Oppé and the Working Party for giving their time and expertise so generously in a matter of such importance for the health of future generations.

**H. YELLOWLEES**

Chairman,

Committee on Medical Aspects of Food Policy



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# I. Introduction

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## 1. General

### 1.1. Background Information

1.1.1. In June 1973 the Committee on Medical Aspects of Food Policy asked the Panel on Child Nutrition to set up a Working Party to review present practice in infant feeding and to make recommendations. The report of the Working Party was accepted by the parent Committee in December 1973 (Department of Health and Social Security, 1974). Two recommendations are of particular relevance to this present report:

- a. "we recommend that the reconstituted artificial feed . . . . . should approximate to the composition of breast milk as nearly as is practicable. Such milk feeds should contain a concentration of phosphate, sodium and protein which is lower than that of cows' milk and nearer to that of breast milk (para 6.3.1, p 25), and
- b. we recommend that the legislation concerning the composition, labelling and advertising of milk-based infant foods be reviewed (para 6.7, p.26)."

1.1.2. At present there are no specific regulations in the United Kingdom to control the composition, description and labelling of infant foods. In England and Wales these foods are however, like all other foods, subject to the general safeguards provided in the Food and Drugs Act (Statutes 1955) and to regulations dealing with additives, contaminants and food labelling; similar legislation applies to Scotland and Northern Ireland. In particular the Skimmed Milk with Non-Milk Fat Regulations (Statutory Instruments 1960) as amended require foods based on skimmed milk with non-milk fat to be labelled 'Unfit for Babies'. Exemption from this requirement is given only to specified foods which the Committee on Medical Aspects of Food Policy advises are suitable for infant feeding. The Lead in Food Regulations (Statutory Instruments 1979) (as amended) establish a maximum limit of 0.2 mg lead/kg of infant food when prepared ready for consumption except for rusks in which the maximum permitted amount of lead will remain at 0.5 mg lead/kg food. The Antioxidants in Food Regulations (Statutory Instruments 1978) prohibit the labelling, description or advertisement of any food as being intended for babies or young children if it has in it or on it butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate, octyl gallate, dodecyl gallate, or ethoxyquin. The Regulations permit the presence of BHA or BHT (or both) at specified amounts in vitamin A preparations which are used in the manufacture of foods that are described as intended for babies or young children.



1.1.3. In April 1974 the Food Standards Committee<sup>1</sup> was invited by Ministers to advise on the need for standards or for other controls on the composition and description of foods for infants and young children. The Food Standards Committee sought advice on the nutritional aspects of its review from the Committee on Medical Aspects of Food Policy, which set up the present Working Party (Membership p.iii) consisting of experts in the fields of paediatrics, nutrition and biochemistry.

## 1.2. Terms of reference

To advise the Food Standards Committee on

- (a) suitable definitions for the terms: baby, infant, young child,
- (b) the nutritional needs of these groups of the population,
- (c) any nutritionally significant limits that should be set for the composition of foods<sup>2</sup> for infants and young children,
- (d) any limitations on the use of specific foods or ingredients,
- (e) any additional factors related to special dietary requirements,
- (f) the use of adult foods and drink which carry instructions on the label that refer to feeding infants or which are promoted for this purpose.

## 1.3. Scope of the Report

1.3.1. The Working Party realised the wide scope of any review of foods for infants and young children and that the review would relate to conditions in the United Kingdom. Early in the discussion of the terms of reference the decision was made to give priority to foods for young infants which may be used instead of human milk as the sole source of nourishment. Only these foods are discussed in this report<sup>3</sup>.

1.3.2. The first part of the report is devoted to a consideration of suitable definitions for the terms baby, infant and young child as required by the first part of the terms of reference, and to a general discussion of those foods for the young infant which use cows' milk protein as the source of nitrogen. The second part of the report is chiefly concerned with the evidence upon which compositional guidelines are set for the energy content and nutrient composition of foods which are intended to provide the sole nourishment for healthy young infants and those who have no special dietary requirements. The difficulties of establishing such guidelines are made clear. Foods which do not use cows' milk

<sup>1</sup>The Food Standards Committee advises the Minister of Agriculture, Fisheries and Food, the Secretary of State for Social Services, the Secretary of State for Scotland, the Secretary of State for Wales and the Head of the Department of Health and Social Services for Northern Ireland on the exercise of their powers under the Food and Drugs Act 1955 and the corresponding enactments relating to Scotland and Northern Ireland, to control the composition and description of food.

<sup>2</sup>'Food' for the purposes of the Food and Drugs Act 1955 includes food and drink.

<sup>3</sup>Appendix 3 discusses milk foods for older infants. These foods would be part of a mixed diet and not the sole source of nourishment.



protein and foods for infants with special dietary requirements are briefly considered in the third part of the report. Part four refers to non-nutritional substances in the foods, the reconstitution of infant feeds and the views of the Working Party on the labelling and advertisement of foods for young infants. Part five of the report includes the summary, conclusions and recommendations.

1.3.3 The report is mainly concerned with artificial feeds for the healthy young infant. Findings from research in the feeding of pre-term infants have provided useful evidence for and information about the desirable composition of feeds for healthy infants.

#### 1.4. **Acknowledgements**

In the preparation of this Report, the Working Party wishes to acknowledge the benefit of helpful discussions with Dr W F J Cuthbertson (Glaxo Group Research Ltd), Dr G A Faux and Miss J Robertson (John Wyeth and Brother, Ltd), Mr R A Hendey (Cow & Gate Ltd) and Mr A E Mettler (Farley Health Products, Ltd).

## 2. **Definitions**

### 2.1. **Baby, infant, young child**

2.1.1. The word 'baby' is a term which is universally recognized but is applied to an ill-defined age group. There was agreement that no attempt should be made to give it a precise meaning for the purposes of this report. There is no objection to the term being used on labels or in informative statements about foods but it should not be used in regulations.

2.1.2. The first year of life is a period of rapid growth and development but the changes in nutritional requirements which accompany growth are gradual. There is no identifiable age at which these changes occur and individual infants who are of the same age or have the same weight may differ in their daily nutrient requirements.

2.1.3. Nevertheless, an age basis appears to be of more practical use for definitions than one based on weight. The United Kingdom recommended daily amounts (RDA) for energy (Department of Health and Social Security, 1979), which apply to groups of healthy infants, are stated for the trimesters 0-3, 3-6, 6-9, 9-12 months. The eighth edition of the recommended dietary allowances published by the United States of America (National Academy of Sciences, 1974) divides the first year of life into two periods: 0-6 and 6-12 months. In addition, for many years morbidity and mortality statistics have been based on the definition of an infant as a person who has not attained the age of one year. This definition of an infant is accepted, although there are no



clearly defined or abrupt physiological changes at one year which would necessitate a sudden change in the kinds of food required.

2.1.4. Low birthweight infants whose birthweight is 2500 g or less are in a special category. In the neonatal period and sometimes for some weeks after birth, low birthweight infants need medical supervision and have special dietary requirements. In due course as growth occurs the requirements of infants who were of low birthweight are in most respects similar to those of other infants.

2.1.5. There is no widely accepted definition of the term 'young child' but the term can be used to describe a child from the age of one to three years.

## 2.2. Statement of definitions

2.2.1. The following definitions will be used:

An *infant* is a child who has not attained the age of one year.

A *young child* is a child aged from one to three years.

## 2.3. Terms used in the Report

2.3.1. Breast feeding is the natural method of feeding and human milk is the natural food for an infant in the first few months of life. The term 'young infant' is used when the sole source of nourishment should be either human milk or a suitable alternative. 'Older infants' are those who require other foods in addition to human milk or the suitable alternative.

2.3.2. In the United Kingdom the terms *artificial food* and *artificial feeding* are in common use and, from the derivation of the word artificial<sup>1</sup>, can be recommended because foods derived from cows' milk, the milk of any other mammal or from plant sources are not the 'natural' food for the human infant. *Human milk substitute* is not used because it suggests that a substitute exists which is in all respects equal to human milk. This is not so and the belief that any artificial food can, at present, be considered as the exact equivalent of human milk should not be encouraged. The term *infant formula* is not as widely used in this country as in the United States of America and some other countries. Nevertheless, the term has international recognition among English speaking nations and has been adopted in this report.

2.3.3. The term *infant formula* refers to the manufactured product which may be ready-to-feed, a concentrated liquid or a dry powder and, after reconstitution, can be used as the sole source of nourishment for the young infant. Infant formula can also be used, as can human milk, in conjunction with other foods for older infants.

<sup>1</sup>The Oxford dictionary defines 'artifice' as a device, contrivance or skill, and 'artificial' as not natural.



2.3.4. *Special infant formula* refers to a product which is manufactured for infants who require a diet which, for medical reasons, is different from that of healthy infants.

2.3.5. The term *feed* refers to the product as fed to the infant. An artificial feed is prepared by the reconstitution of infant formula (or special infant formula) with water according to the manufacturers' instructions, and can be used as the sole source of nourishment for the young infant. Such feeds can be considered as modified, processed and fortified with certain nutrients.

### 3. Foods for the young infant

#### 3.1. General considerations

3.1.1. The new born infant undergoes a complex series of adaptive changes which affect all body systems when the placental alimentation of fetal life is replaced by gastro-intestinal nutrition. The transition is usually accomplished within the first few days but may take longer. The infant is born with stores of various nutrients in differing amounts and these must be taken into account when nutritional requirements are considered. Human colostrum and human milk are the foods which best meet the needs of the young human infant but any inadequacy of lactation makes it imperative for some alternative to be available.

3.1.2. Young infants vary in their individual needs for nutrients and are subject to changes in requirements associated with environmental conditions and illness. Nutritional requirements in exact quantitative amounts of individual nutrients are incompletely known but it seems reasonable to use the composition of human milk as an indicator for the desirable composition of infant feeds. There are, however, difficulties. The composition of colostrum, transitional, and mature human milk is not constant. Milk from any one mother varies in composition from one breast to the other, from the beginning to the end of the feed, from one feed to another during the day and over the course of lactation. The composition depends also to some extent on the maternal diet. The extent to which the differences are of biological importance has not been determined, but it is clearly impossible for any artificial feed to allow for the variations in composition which have been found in human milk.

3.1.3. It is by no means certain that all the constituents of human milk which have biological importance have as yet been identified, or indeed that all the known constituents play an essential part in the well-being of the infant.

3.1.4. Some constituents of biological importance, among which are living cells, lactoferrin, the immunoglobulins, bifidus factor and certain enzymes (Goldman and Smith, 1973; Downham, Scott, Sims, Webb and Gardner, 1976; Schlesinger and Corelli, 1977; Robinson, Harvey and Soothill, 1978; McClelland, McGrath



and Samson, 1978) are not included in manufactured infant milk foods. Thus a product which has a chemical composition similar in some, or even in most, respects to human milk is not necessarily biologically equivalent in its nutritional value and physiological characteristics.

3.1.5. Although human milk, because of its variability, cannot be used as an exact chemical model for the composition of an infant feed, the Working Party is of the opinion that human milk does provide the most useful reference 'standard'. The further the composition of any artificial feed departs from that of average mature human milk, the greater is the possibility of untoward effects in the infant to whom it is fed. It is important to ensure that infants are safeguarded from unsuitable feeds.

3.1.6. With this in mind, the average composition of mature human milk obtained from mothers in the United Kingdom was compared with the composition given in previous publications which are usually regarded as standard works. Pooled samples of mature human milk were obtained from five centres in Great Britain and were analysed by the Laboratory of the Government Chemist (Department of Health and Social Security, 1977). As expected, there were variations in composition from one area to another and had individual samples of milk been analysed the range of nutrient composition would undoubtedly have been greater. The analytical results differed little from those of earlier workers in spite of advances in laboratory techniques. The Working Party was of the opinion that the analyses could be used with some confidence in attempting to develop guidelines for the composition of products to be used in artificial feeding of healthy infants. In the present report frequent reference is made to the results of these analyses and also to the published results of earlier workers.

3.1.7. Recommendations for the composition of infant formulae have recently been made by several expert bodies, for example the American Academy of Pediatrics, Committee on Nutrition (1976), the Food and Agriculture Organisation/World Health Organisation (FAO/WHO) Codex Alimentarius Committee on Foods for Special Dietary Purposes (1976) and the European Society of Paediatric Gastro-enterology and Nutrition (ESPGAN 1977). These recommendations have been considered by the Working Party.

3.1.8. The proposed guidelines have taken into account the experience gained in the use of well-tried foods which are at present available in the United Kingdom for the young infant and the impossibility of producing a food which can simulate human milk in all respects. Clinical and scientific investigations of the physiology and pathology of infants in relation to feeding and other relevant studies have also been an important source of evidence. For many nutrients, such as the trace elements, present knowledge is incomplete and there is also only suggestive evidence about the possible subtle and long-term effects of deficiency, excess or imbalance of nutrients.

3.1.9. The composition of an infant formula may be considered at different stages in the chain from raw materials to the feeding bottle. These are (a) the



stage of manufacture, (b) the point of distribution or sale to the purchaser and (c) the reconstituted feed as given to the infant. This report is concerned with the composition of the reconstituted feed when prepared according to the instructions given by the manufacturer.

3.1.10. Some foods are marketed as ready-to-feed but the majority are manufactured and sold as powders or as concentrated liquids which require to be reconstituted with water. The final composition of the reconstituted feed is affected by any substances present in the water (para 4.9).

3.1.11. Instructions given to the purchaser about the reconstitution of infant feeds should be easily understood so that whoever is responsible for reconstitution can follow them and prepare the feed correctly. The problems associated with the size of scoops for measuring dry powders, labelling instructions and the information given in promotional literature are therefore important and have been considered where such matters impinge on nutritional advice.

3.1.12. It is well known that the requirements for energy and for nutrients vary widely between individual infants whether breast-fed or artificially fed. When feeds of standard composition are offered the daily intake of nutrients can be regulated only by changing the volume of the feed. The healthy breast-fed infant, whose mother has an adequate supply of milk, can more easily regulate the intake than can the artificially-fed infant whose mother may deliberately attempt to give a measured volume at each feeding time. It is therefore important that mothers and their advisers are made fully aware of the need to take individual differences into account when feeding young infants.

3.1.13. Food additives and contaminants are the concern of the Food Additives and Contaminants Committee<sup>1</sup>, and of the Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment<sup>2</sup> (formerly the Toxicity Sub-Committee of the Committee on Medical Aspects of Chemicals in Food and the Environment). These substances are referred to in paras 17.1 to 17.3 of this report.

## **3.2. Criteria for foods for the young infant**

3.2.1. If a manufactured food is to be used instead of human milk it should be convenient for the mother to obtain and to store. It should also be easy to

<sup>1</sup>The Food Additives and Contaminants Committee advises the Minister of Agriculture, Fisheries and Food, the Secretary of State for Social Services, the Secretary of State for Scotland, the Secretary of State for Wales and the Head of the Department of Health and Social Services for Northern Ireland on matters referred to them by Ministers in relation to food contaminants, additives and similar substances which are or may be present in food or used in its preparation.

<sup>2</sup>The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment advises, on request, on the hazards to health including toxicological and carcinogenic risks, which result from the use of or presence of additives, contaminants or pesticides in food and in the environment.



reconstitute accurately and, when reconstituted, must be acceptable to the infant. Certain nutritional qualities are also essential. When correctly prepared and given to the infant in adequate volume, the reconstituted feed should

- (a) promote growth and development, and maintain a physiological state which is as close as possible to that of the healthy breast-fed infant,
- (b) be of such composition that it can be used as the sole food for young infants (para 2.3.1),
- (c) be such that the nutritional needs of the growing infant are met by progressive increases in the volume of the feed rather than by increases in its concentration or the addition of supplementary nutrients.
- (d) contain no ingredients in amounts which are toxic,
- (e) be free from harmful micro-organisms,
- (f) have minimal potential for allergic reactions, and
- (g) contain the minimum number of food additives taking into account the recommendations of the Food Additives and Contaminants Committee and the Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment.

### 3.3. Compositional guidelines

3.3.1. In practice it is difficult to apply all these criteria to foods for the young infant because

- (a) precise comprehensive knowledge of the nutritional requirements for growth and development of young infants is lacking,
- (b) the relative importance of nutritional compared with other factors, both genetic and environmental, which influence growth and health is not fully understood and
- (c) the effects of processing and storage on the nutritional value of artificial foods are not fully known.

3.3.2. Infants must, however, be safeguarded from any food which is nutritionally unsuitable or which could cause damage to health. It is only within the last 25 years that the physiology of young infants has been more extensively investigated and paediatricians have become aware of hitherto unrecognized risks to health, in both the short and long term, which may occur from the use of artificial foods. For this reason the Working Party believes that an attempt should be made to define compositional guidelines within the limits imposed by existing knowledge and the practicability of modern technology. These guidelines, if applied, should at least ensure that foods intended to be used instead of human milk are suitable nutritionally and carry no unacceptable health risks.

3.3.3. The term compositional *guidelines* is used rather than a compositional *standard* because present knowledge is insufficiently advanced for exact recommendations to be made in relation to every component of a food which



will meet the needs of the majority of young infants or even, as is the case for the trace elements, of making any recommendation other than that the nutrient in question should be present. Nevertheless, upper and lower limits for the concentration of most nutrients are proposed. Consideration has been given both to the variability in composition of mature human milk and to the composition of foods which are at present available. The guidelines also permit the flexibility which is necessary for the development of new products as further advances in knowledge are made.

### **3.4. Nutritional evaluation of foods for the young infant**

3.4.1. Foods which may seem, in the light of present knowledge and experience, to be acceptable in composition might nevertheless later be shown to be unsuitable as a substitute for human milk. Some essential nutrient, as yet unrecognized and therefore not included in the compositional guidelines, might be absent or deficient or lost in processing, with the result that the biological effects could be different from those expected when nutrient composition alone is considered. In addition there may be problems of the bioavailability of individual nutrients and of nutrient imbalance. Clinical and biological evaluation of all products is therefore necessary, and is indeed present practice. Most manufacturers make thorough trials before introducing either new foods or modifications of those already in production.

3.4.2. The simplest form of clinical testing is the systematic observation of a selected group of infants in respect of factors associated with acceptability and tolerance of the product. The eagerness with which the feed is taken, the occurrence of vomiting or regurgitation, the frequency and characteristics of the stools, and the presence or absence of excoriation of the buttocks are examples of items of information which are pertinent. The value of such observation is enhanced by random selection of a sample which is large enough to reveal infrequent problems by comparison with control groups of breast-fed infants. Collection of the information described should involve little or no disturbance to the infant and be ethically unobjectionable.

3.4.3. More refined studies include systematic measurements of growth, but may be hampered by the need to employ trained observers. There are also difficulties in the interpretation of results. There is no precise definition of optimal growth, and maximal gain in weight may not necessarily be optimal. Nevertheless, it should be possible to detect failure to thrive or early obesity by comparison with the growth rates of breast-fed infants. Feeding trials present many difficulties but should be continued for an appropriate length of time and not only for the first few weeks of life since the product is to be the sole source of nourishment for several months.

3.4.4. Clinical and physiological investigations into the special characteristics of infants with regard to digestion, absorption, renal excretion and metabolism of individual nutrients and of the diet as a whole have led to greatly increased knowledge of infant physiology and nutrition. Much of this knowledge, which



has been derived from studies of human infants and the young of other mammals, is relevant to the composition of infant formulae. Metabolic balances and investigations of blood composition may be needed in order to verify the suitability of artificial foods. There is no single analysis or study which would confirm that a newly developed food, or variation of an existing food, has a biological effect which is equivalent to that predicted from its nutrient composition or from the results of simple feeding trials (para 3.4.2). Because of the skills required and the ethical considerations involved, it is important that there should be the fullest co-operation not only between mothers and babies and paediatricians, but also with industry, academic departments of nutrition and paediatrics, and regulatory bodies.

3.4.5. Foods for the young infant which are at present in use have mostly been well-tried. It is therefore likely that any adverse effects of new variations of these foods would be subtle and not easily detected. Such effects might be related to differences in gut flora, differences in immunoglobulins or to allergic reactions and would probably be less susceptible to testing by routine trials and be recognized only in the long term. Developments in food technology or the use of new raw materials may result in products which differ in fundamental respects from existing foods for young infants. Such products should receive close scrutiny and be subject to extensive trials.

3.4.6. Assessment of the suitability and safety of an infant formula should include consideration of

- (a) the ingredients used,
- (b) comparison with the proposed compositional guidelines,
- (c) laboratory tests and animal trials to assess nutritional adequacy and, for example, protein quality if appropriate,
- (d) feeding trials with human infants of appropriate age to provide evidence regarding acceptability, tolerance, nutritional adequacy and freedom from adverse effects,
- (e) metabolic studies when these are appropriate,
- (f) evaluation of any clinical or scientific information which suggests an association between the infant food or its constituents and disease, and
- (g) microbiological testing to ensure that the food is free from harmful organisms.

3.4.7. The testing outlined above should be undertaken by the manufacturer, who will require to work closely with paediatricians and possibly to consult with a scrutiny panel concerning the evaluation of his product and the degree of testing required.

### **3.5. Scrutiny of foods for the young infant**

3.5.1. At present the only products intended for infant feeding which come under pre-marketing scrutiny, apart from the general safeguards of the Food

and Drugs Act 1955, are those based on cows' milk from which all the fat has been removed and replaced by non-milk fat (para 1.1.2). Only when an expert panel of the Committee on Medical Aspects of Food Policy is satisfied that such a product is suitable for infant feeding can the manufacturer gain exemption from a legal requirement to label such foods as 'unfit for babies'.

3.5.2. A food which in energy content and nutrient composition complies with the guidelines suggested in this report need not necessarily satisfy the nutritional requirements of the young infant (paras 3.4.1 and 4.7). The Working Party is therefore of the opinion that any food which is manufactured as the sole source of nourishment for the young infant should be subjected to scrutiny by an expert panel.

3.5.3. The Scrutiny Panel would have the task of assessing the evidence supplied by manufacturers in order to consider for approval any products which are intended for sale as the sole source of nourishment for young infants. The Panel could also require further tests, or an independent verification of tests, where necessary.

3.5.4. Were such scrutiny practised, and the only foods marketed as suitable for young infants were those accepted by the expert Panel, those who have the care of young infants would know that every possible step had been taken to ensure that any food on sale for young infants would be nutritionally suitable and microbiologically and toxicologically safe. It is outside the terms of reference of the Working Party to consider how a system of scrutiny and control would be implemented.



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## II The energy and nutrient content of infant feeds

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### 4. General principles

4.1. In attempting to set compositional guidelines for foods for the young infant, present knowledge about the nutritional requirements of these infants has been considered. This knowledge is derived from several sources:

- (a) chiefly from what is known about the composition of human milk;
- (b) comparison with what is known about the requirements of adults and young children;
- (c) metabolic and other physiological studies, including balance studies, with either human milk or any of the artificial milks at present in use, which provide information about the ability of young infants to absorb certain nutrients;
- (d) information about disease in relation to infant feeding;
- (e) information derived from experience with parenteral nutrition, and
- (f) published opinions of experts on the nutritional requirements of infants.

4.2. The primary concern of the Working Party was the composition of the feed as offered to the infant. The choice of a standard volume rather than a standard energy value seemed more appropriate and more useful to the mother and to her professional adviser. The guidelines are therefore expressed in amounts per 100 ml feed as reconstituted and ready to be consumed. This underlines the importance of water as an essential nutrient. Reference to a standard volume is also preferable because it does not involve assumptions about the available energy of nutrients and eliminates the problem of expressing nutrient composition over a range of energy values. However, in order to facilitate comparison with other published reports, the compositional guidelines in this report are set out for three different energy values in Appendix 2.

4.3. For each nutrient an attempt has been made to give a reasoned argument which would support a suggested range of concentration<sup>1</sup>. As far as is possible the arguments have been set out in a standard manner:

<sup>1</sup>Problems about the inclusion of 'overages', that is to say amounts over and above the upper limit guidelines for any particular nutrient in order to ensure that at least the lower limit would be met after the normal shelf life, would be discussed between the manufacturer and the Scrutiny Panel.



- (a) the concentrations of the nutrient found in the majority of samples of human and cows' milk,
- (b) nutritional information derived from the use of the unmodified cows' milk products (now no longer available) and the use of the present products in infant feeding,
- (c) a discussion of the suggested upper and lower limits for the amount of each nutrient/100 ml of reconstituted feed,
- (d) any relevant information about the chemical, physical and biological characteristics of the nutrient, and
- (e) recommendation(s).

A similar procedure has been adopted for energy.

4.4. For some nutrients there is evidence to support the conclusions with some conviction; for others the evidence is less definite, and for yet others there has been little or no experimental investigation so that either arguments based on the composition of human milk have been put forward or no firm recommendation has been made.

4.5. Lower limits must be set in order to prevent under-nutrition. To set an upper limit is often equally desirable in order to avoid the harmful effects which, in the case of some nutrients, may result from an excessive intake. The evidence for upper and lower limits is often somewhat tenuous.

4.6. By defining upper and lower limits for the concentrations of any one nutrient, limits may be automatically imposed for some other nutrient. For example, the amounts of vitamin E and polyunsaturated fatty acids are interdependent (paras 8.18 and 9.2.3.4).

4.7. Because of the very wide ranges for the concentration of some nutrients in individual samples of human milk, there is the possibility that many such samples of human milk would not satisfy the compositional guidelines set by the Working Party in respect of every nutrient. In addition, it might be possible theoretically to produce a formula which is within the compositional guidelines and yet is not a suitable food because the relative proportions (or balance) of nutrients is unsatisfactory. This emphasizes the need for careful assessment of the biological properties of feeds and for assessment of the manufacturer's evidence by a scrutiny panel.

4.8. Infant feeds are usually reconstituted by the addition of water. In order to minimize mistakes in reconstitution it is desirable that nothing but water should be added to the dry powder or concentrated liquid.

4.9. The mineral content of household water varies with the source of supply and can be altered by domestic water softeners or by prolonged boiling. The addition of water which has been freshly boiled and then cooled should be used



in the reconstitution of milk powders or concentrated liquids. Water which has been softened by means of a domestic water softener should not be used in the reconstitution of infant feeds.

## 5. Energy

5.1. *Introduction.* The metabolizable (available) energy value of a food is usually calculated from its chemical composition using one of a series of energy conversion factors. In this report energy values in kilocalories (kcal) have been calculated using the modified Atwater factors derived from the studies of Southgate and Durnin (1970); values expressed in kilojoules (kJ) are obtained using the factors suggested by The Royal Society (1972) and are used in the Labelling of Food Regulations (Statutory Instruments 1970). The two series of factors<sup>1</sup> are as follows:

carbohydrate (expressed as the monosaccharide or as lactose monohydrate) <sup>2</sup>	3.75 kcal/g	16 kJ/g
protein (total N g x 6.38)	4 kcal/g	17 kJ/g
fat	9 kcal/g	37 kJ/g

The above factors were derived from studies of adults who ate mixed diets and are therefore not necessarily applicable to young infants who consume only milk. The differences involved are small and are discussed in the following paragraphs.

5.2. In the first place there are differences in the gross energy values of the constituents of different foods. All energy conversion factors are calculated from gross energy values, that is to say, heats of combustion. The values used for mixed diets are usually composite values, for example the gross energy of fat is taken as 9.35 kcal/g. The heat of combustion of a fat, however, depends on the fatty acid composition. Thus the heat of combustion of human milk fat is greater (9.37 kcal/g) than that of cows' milk fat (9.19 kcal/g) because human milk fat contains less of the short chain fatty acids (para 8.3). Small differences can also be expected between the heats of combustion of the protein of the two milks because of differences in amino acid composition (para 6.8). In this report, except in Tables 1 and 1A, protein has been calculated by multiplying total nitrogen by the factor 6.38 (paras 6.1 to 6.3).

5.3. Secondly, in the derivation of the Atwater protein factor (Merrill and Watt, 1955) there is a correction for the energy lost by the excretion of nitrogenous compounds in the urine on the assumption that the adult subject is

<sup>1</sup>1 kilocalorie is equivalent to 4.184 kilojoules. The figures in the two series of factors are not precisely equivalent because they have been rounded from experimental values.

<sup>2</sup>When expressed as monosaccharide, 100 g lactose is equivalent to 100 g lactose monohydrate or 95 g anhydrous lactose.



in nitrogen balance. A healthy young infant grows rapidly and retains nitrogen. The derivation of the factor is therefore more complex (Southgate and Barrett, 1966). The true value for the protein energy factor varies according to the proportion of the nitrogen intake which is retained.

5.4. Energy conversion factors, by correcting for the loss of energy in faeces, allow for the fact that the different food constituents are not completely digested and absorbed. The apparent digestibilities of the protein, carbohydrate and fat of milk when determined for infants who were 14 days old (Southgate and Barrett, 1966) were different from those observed for adults (Southgate and Durnin, 1970). There were also significant differences in the apparent digestibilities and therefore in the derived energy conversion factors depending on whether the infants were fed human milk or preparations of cows' milk (Table 5.1).

**Table 5.1:** *The apparent digestibility<sup>1</sup> and the derived energy conversion factors for infants aged 14 days who were fed either human milk or artificial feeds based on unmodified cows' milk.*

Nutrient	Milk	Apparent digestibility per cent	Energy Conversion factor – kcal/g
Protein	human milk	82.1	4.39 <sup>2</sup>
	cows' milk preparations	89.2	4.74 <sup>2</sup>
Carbohydrate expressed as monosaccharide	human milk	96.9	3.64
	cows' milk preparations	99.9	3.76
Fat	human milk	94.5	8.74
	cows' milk preparations	85.4	7.90

Source: From Southgate and Barrett (1966) with carbohydrate values recalculated.

<sup>1</sup>Apparent digestibility of a food (or food constituent) is the difference between the amount ingested and the amount excreted in the faeces expressed as a percentage of the intake.

<sup>2</sup>The derivation of these factors is discussed by Southgate and Barrett (1966).

5.5 There is evidence that the apparent digestibility of fat in milk improves as the infant develops (Widdowson, 1965) and therefore the use of a single conversion factor for fat throughout the first six months of life is also not strictly valid.

5.6. *Human and cows' milk.* There are few studies of young infants which provide information from which energy conversion factors can be derived. If the factors derived by Southgate and Barrett (1966) and the modified Atwater factors of Southgate and Durnin (1970) are applied to human milk and unprocessed cows' milk which have the average composition shown in Table 1 (Appendix 1), the calculated energy values for the two milks are as follows;



	Southgate and Barrett (1966)	Southgate and Durnin (1970)
human milk	69.7 kcal/100 ml	69.6 kcal/100 ml
cows' milk	65.1 kcal/100 ml	65.4 kcal/100 ml

5.7. These calculations show that the errors involved in using factors derived from studies with adults are small. This is because the energy conversion factor for protein is higher and that for fat lower in infants than in adults.

5.8. *Nutritional considerations.* Energy requirements vary from one infant to another, and can be very different even if two infants are of the same age and weight, and are growing at the same rate. Energy intake depends on the volume and number of feeds and on the amounts of carbohydrate, protein and fat which are absorbed.

5.9. In successful breast-feeding the infant is usually fed on demand and the amount of food consumed is largely determined by the infant but bottle-fed infants may often be encouraged to take all the reconstituted feed in the bottle. There is little information about the amount of milk consumed by infants who are exclusively breast-fed, but there is evidence to suggest that the weight gain of bottle-fed infants is either similar to or greater than that of breast-fed infants (Mellander, Valquist and Mellbin, 1959; Fomon, Thomas, Filer, Ziegler and Leonard 1971; de Swiet, Fayers and Cooper, 1977). Fomon (1974) showed that after 41 days of age infants were able to regulate the volume ingested in such a way that total energy consumption was the same whether a low or high energy milk was given, but younger infants who were fed a 'low-energy' milk had a smaller total energy intake than those given a 'high-energy' milk. The findings suggest that younger infants who were given a 'low-energy' milk achieved a near maximal volume of intake and it should not be assumed that infants who are fed a dilute milk before the age of about six weeks can ingest a sufficient volume to meet their energy needs.

5.10. *Upper and lower limits for the energy value of infant formula.* Macy, Kelly and Sloan (1953) reported a range of means from the literature for the energy value of human milk to be 67–75 kcal/100 ml. Macy and Kelly (1961) published the mean of these mean values as 71 kcal/100 ml compared with a mean of their own values for individual samples of 75 kcal, the range for their individual samples being 45–119 kcal/100 ml. Kon and Mawson (1950) reported mean values of 76 and 70 kcal, Morrison (1952) 64 kcal, McCance and Widdowson (1967) 80 kcal and Fomon (1974) 75 kcal/100 ml. The observed mean energy value of the five pooled samples of mature human milk which were recently analysed varied from 65–75 kcal or 270–315 kJ/100 ml<sup>1</sup> (Department of Health and Social Security, 1977) although individual samples of human milk would certainly have had an energy content outside the range for pooled samples. Even though individual samples of human milk may well yield less or more energy, the energy content of an artificial feed should be

<sup>1</sup>energy values expressed in kilojoules are rounded to the nearest 5kJ.



close to the mean for average human milk, that is to say, 70 kcal (295 kJ) with a lower limit of 65 kcal (270 kJ)/100 ml feed and, because of the potential risks of over-feeding, an upper limit of 75 kcal or 315 kJ/100 ml.

#### 5.11. *Recommendation.*

We recommend that the calculated energy value of any infant formula should be within the range of 65–75 kcal or 270–315 kJ/100 ml of reconstituted feed.

## 6. Protein

6.1. *Introduction* The amount of protein in a food is customarily expressed by multiplying the figure for the total nitrogen in the food by a given factor. The factor varies with the amino acid composition of the protein. For milk and milk products the factor is 6.38 (FAO/WHO, 1973). Mature human and cows' milk contain similar concentrations (40–50 mg/100 ml) of non-protein non-amino acid nitrogen and, because the total amount of nitrogen in human milk (210 mg/100 ml) is much less than in cows' milk (540 mg/100 ml), multiplication of the total amount of nitrogen in human milk by the factor 6.38 results in over-estimation of the actual amount of protein in human milk by some 20 per cent (Lönnerdal, Forsum and Hambræus, 1976). The error which results from calculating the total amount of protein in cows' milk by multiplication of the figure for total nitrogen by 6.38 is smaller (some 7–10 per cent) and is usually ignored. The protein content of human milk shown in Table 1 is therefore shown both as crude protein (total N x 6.38) and true protein calculated from the total amino acid nitrogen x 6.38.

6.2. *Human and cows' milk protein* The mean value for the total nitrogen content of pooled samples of mature human milk (Table 1) was 0.21 g/100 ml. This is equivalent to  $0.21 \times 6.38 = 1.34$  g protein/100 ml. After correction for the non-protein non-amino acid nitrogen (para 6.1) the true protein content was 1.05 g/100 ml. A representative value for cows' milk is 0.54 g total nitrogen/100 ml which is equivalent to 3.44 g protein/100 ml. When allowance is made for the non-protein non-amino acid nitrogen of cows' milk (para 6.1) the protein in cows' milk provides approximately 16 per cent of the total energy whereas the protein of human milk provides only 6 per cent of the total energy.

6.3. In this report, the more accurate calculation in which total amino acid nitrogen is multiplied by 6.38 has been used only for quoting the true protein content of average mature human milk in Tables 1 and 1A. Other calculations of the apparent digestibility of proteins, discussions about protein quality, amino acid composition and the upper and lower limits for the amount of protein suggested in the guidelines for the composition of the reconstituted artificial feed have been based on the figure for protein obtained in the conventional way by multiplying the total amount of nitrogen by a factor which, for milk protein, is 6.38 and for most other proteins is 6.25.



6.4. The proteins of colostrum and milk are distinctive (Tables 6.1). Casein (a mixture of caseins) occurs in both human and cows' milk and these proteins are among the few naturally occurring phospho-proteins. The remaining milk proteins are collectively called whey proteins. Milk has the property of clotting in the stomach to form curd which consists of modified caseins, milk fat and some of the whey proteins and is slowly digested. In human milk casein makes up about 40 per cent of the total protein and the whey proteins about 60 per cent. Cows' milk has about 80 per cent casein and 20 per cent whey proteins.

6.5. Whey proteins are a mixture of soluble proteins. Typical amounts of the component proteins in human and cows' colostrum and mature milk are shown in Table 6.1 from which it is evident that  $\beta$ -lactoglobulin is the predominant whey protein of cows' milk but human milk contains relatively more  $\alpha$ -lactalbumin and no  $\beta$ -lactoglobulin. Both milks contain serum albumin. The whey of human milk contains lactoferrin but there is little or none in cows' milk. Whey proteins also include traces of lysozyme and other enzymes (Mackenzie, 1970; Ogra, Wintraub and Ogra, 1977; McClelland, McGrath and Samson, 1978).

6.6. Colostrum and early lactation milk contain relatively large concentrations of immunoglobulins. On average 50 per cent of the protein of human colostrum is secretory Immunoglobulin A but in mature milk only about 14 per cent of the protein is Immunoglobulin A (Table 6.1). More than three-quarters of ingested Immunoglobulin A is excreted in the infant stool (Ogra, Weintraub and Ogra, 1977; McClelland, McGrath and Samson, 1978).

**Table 6.1:** Average composition of the protein in human colostrum on the second day, in mature human milk, and in cows' colostrum and milk.

	COLOSTRUM		MATURE MILK	
	Amount g/l	Percentage of total protein	Amount g/l	Percentage of total protein
<b>HUMAN</b>				
Total protein	100	100	11	100
caseins	(16)	(16)	4.5	41
$\alpha$ -lactalbumin	(11)	(11)	3.1	28
lactoferrin	14	14	1.5	14
serum albumin	1.6	1.6	0.3	2
lysozyme	0.4	0.4	0.1	1
immunoglobulin (IgA)	54	54	1.5	14
<b>COWS'</b>				
Total protein	65	100	33	100
caseins	35	54	26	79
immunoglobulins	19	29	1.0	3
$\beta$ -lactoglobulin	3	5	3	9
$\alpha$ -lactalbumin	3	5	1.2	3.5
serum albumin	1	1	0.3	1
other proteins	4	6	1.5	4.5

Source: Bezkorovainy, 1977. Jennes, 1974. Lönnerdal, Forsum and Hambraeus, 1976. McClelland, McGrath and Samson, 1978.

Figures in brackets are estimated amounts

6.7. *Nutritional considerations—protein quantity.* The first six weeks of life is the period of most rapid infant growth, and human milk fully satisfies the need for protein provided that the volume of milk is adequate. After this period the proportion of protein required for growth declines, and the proportion needed for tissue maturation and maintenance increases. Provided that the protein quality of an infant feed is maintained, it is desirable that the concentration of protein should be less than that of cows' milk. There is some evidence that a high concentration of some amino acids in the blood may cause neurological damage in premature infants during the post-natal period (Menkes, Welcher, Levi, Dallas and Gretskey, 1972; Goldman, Goldman, Kaufman and Liebman, 1973). In young infants the relatively high protein intake from some artificial foods which were based on whole cows' milk was associated with an abnormally high renal osmolar load and an increase in the amino acid and urea concentration in the blood (Davies and Saunders, 1973). Such foods are no longer advised for feeding young infants and are not now marketed in the United Kingdom.

6.8. *Protein quality — amino acid composition.* The amino acid composition of cows' milk differs from that of human milk in both essential and non-essential amino acids. Table 6.2 shows the composition from some recent analyses.

**Table 6.2:** *The essential amino acids of human and cows' milk<sup>1</sup> (expressed as mg amino acid per g total nitrogen)*

Amino acid	Human milk	Cows' milk
Isoleucine	320	350
Leucine	580	640
Lysine	430	510
Methionine	91	180
Cystine	120	60
Phenylalanine	230	340
Tyrosine	180	280
Threonine	275	310
Tryptophan	140	90
Valine	415	460
Histidine	150	190

Source: Department of Health and Social Security (1977).  
Paul and Southgate (1978).

<sup>1</sup>It is important to recognize that there are discrepancies between different reports of the amino acid composition of both human and cows' milk. These differences may be genuine or they may be analytical artefacts; they do, however, affect the numerical values for amino acid scores and their interpretation. These discrepancies arise particularly for cystine and tryptophan which are the most difficult amino acids to measure accurately but the values reported for threonine and isoleucine are also variable. The values given in the above table are all of the same order as accepted values found in the literature.

<sup>2</sup>Methionine and cystine values are often combined to give total sulphur containing amino acids when computing amino acid scores.

<sup>3</sup>Phenylalanine and tyrosine are similarly combined to give total aromatic amino acid values.



6.9. Comparison of the essential amino acid patterns with the most recent amino acid reference pattern suggested by the FAO/WHO expert group in 1973 shows that both milks have amino acid scores of 100 or more but, because of the higher scores for some amino acids, cows' milk appears to be superior to human milk (Table 6.3). This, however, is not borne out in biological studies. The FAO/WHO (1973) expert group stated that the most appropriate reference amino acid pattern for the assessment of foods for the young infant is at present uncertain. It is unlikely however that human milk is deficient in one of the essential amino acids and we are of the opinion that the amino acid composition of an infant food should be compared with that of the available amino acids of human milk when the nutritional value of the food is being considered.

**Table 6.3:** Comparison of the essential amino acid patterns of human milk and of cows' milk with the suggested FAO/WHO (1973) reference pattern for an ideal protein.<sup>1</sup>

Amino acid	Human milk as % of reference protein	Cows' milk as % of reference protein
Isoleucine	150	160
Leucine	110	130
Lysine	130	150
Methionine + cystine	110	130
Phenylalanine + tyrosine	100	160
Threonine	100	110
Tryptophan	260	170
Valine	140	150

<sup>1</sup>In this table the amounts of amino acids (expressed as mg/g nitrogen) shown in Table 6.2 have been calculated as a percentage of the reference values given in FAO/WHO, 1973.

6.10. The amino acid composition of cows' milk (Table 6.2) shows that two essential amino acids, cysteine and tryptophan, are present at much smaller concentrations/g nitrogen than in human milk. It is necessary therefore to consider whether these differences are of nutritional significance.

6.11. *Cysteine.* The adult can readily synthesize cysteine from methionine, and cysteine should not be considered an essential amino acid for adults. One of the enzymes involved in this conversion, cystathionase, has not been detected in the liver of new-born infants and the activity of another of the enzymes involved, cystathione synthetase, is only about 25 per cent of that found in a child aged 2½ years (Räihä, 1971; Gaull, Sturman and Räihä, 1972). The age at which these enzymes become effective in the young infant is not at present known, and the length of the period after birth during which cysteine should be regarded as an essential amino acid has, therefore, still to be established.

6.12. If the amount of protein (total N x 6.38) in an infant feed were reduced to 1.5 g/100 ml and the protein were unmodified cows' milk protein, that is to say, no alteration in the casein: whey protein ratio has been made, the amount of cysteine would be less than the total provided by human milk (Table 6.4).

**Table 6.4:** Comparison of the amino acid content<sup>1</sup> (mg/100 ml milk) of cows' milk based formula containing 1.5 g protein<sup>2</sup>/100 ml with human milk (1.3 g protein<sup>2</sup>/100 ml).

Amino acid	Cows' milk formula as a percentage of human milk
Isoleucine	131
Leucine	133
Lysine	140
Methionine	239
Cysteine	67
Phenylalanine	183
Tyrosine	186
Threonine	135
Tryptophan	75
Valine	133
Histidine	166

<sup>1</sup>Calculated values derived from the composition given in Table 6.2

<sup>2</sup>Total N x 6.38

The amount of cysteine could be increased by increasing the proportion of whey proteins relative to casein (Table 6.5). Two studies of low birth-weight

**Table 6.5:** The calculated<sup>1</sup> amounts of total sulphur amino acids and cystine (expressed as mg/100 ml milk) in relation to different proportions of caseins and whey protein in a reconstituted cows' milk formula which contained 1.5 g protein per 100 ml feed.

% whey	% casein	Cystine mg/100 ml	Total sulphur containing amino acids mg/100 ml
Human milk			
60	40	25	44
Infant feed			
100	0	41	70
80	20	33	65
60	40	26	61
40	60	20	57
Cows' milk			
20	80	13	53

<sup>1</sup>Calculations were based on the amounts of cystine and methionine in cows' milk whey (Ling, Kon and Porter, 1961), and on the composition of casein stated by the Food and Agriculture Organisation (1973).



babies have shown that there may be advantages for an artificial feed to contain as much cysteine as human milk. R ih , Heinonen, Rassin and Gaull (1976) found that metabolic acidosis was then much less frequent and less severe; Berger, Scott, Kenward, Scott and Wharton (1979) found that the low birth-weight babies absorbed more nitrogen and grew more quickly during the early weeks of life.

6.13. *Tryptophan*. A food in which cows' milk protein had been reduced to 1.5 g/100 ml would contain less tryptophan than human milk (Table 6.3). Nevertheless infants who satisfy appetite with such a milk would receive tryptophan considerably in excess of the requirements suggested by FAO/WHO (1973).

6.14. *Taurine*. The importance of taurine to the young infant has recently been described (Gaull, Rassin, R ih  and Heinonen, 1977). During the first weeks after birth the infant conjugates bile acids with taurine, and only gradually changes to the use of glycine. In animal studies taurine has been shown to be rapidly incorporated into the developing brain and has a role in the function of the retina as well as in cardiac function (Knopf, Sturman, Armstrong and Hayes, 1978). A plentiful supply of this amino acid may therefore be important to the human infant. Brueton, Berger, Brown, Ablitt, Iyngkaron and Wharton (1978) have shown that the duodenal bile acids of low birthweight infants who received expressed human milk for the first three weeks of life were conjugated predominantly with taurine, but in the infants who were given feeds which contained little or no taurine, the bile acids were conjugated predominantly with glycine. Taurine can be formed from cysteine by the action of cysteine sulphinic acid decarboxylase, but this conversion is limited in the young infant. Taurine is present in milk as the free amino acid and there is far more of it in human milk than in cows' milk. The amounts of taurine in the pooled samples of human milk which were collected from different areas of Great Britain were 24 mg/gN or 4.8 mg/100 ml milk (Department of Health and Social Security, 1977). These values agree with those reported by Armstrong and Yates (1963) and by Gaull, Rassin, R ih  and Heinonen, (1977). Cows' milk contains negligible quantities of taurine but as yet no harm due to the absence of taurine in artificial feeds has been reported, and there is at present no evidence to suggest that the addition of this amino acid to foods for the young infant is necessary.

6.15. *Allergens*. The proteins of the milk of the cow or of any artificial food are foreign to the human infant. They are therefore potential allergens to some infants although all infant formulae are heat treated and this reduces the allergenicity of milk proteins. Exposure to them at a time when the body's immunological mechanisms are likely to be immature may be a significant factor in the development of chronic allergic illness which can continue into later life (Taylor, Norman, Orgel, Turner, Stokes and Soothill, 1973; Matthew, Taylor, Norman, Turner and Soothill, 1977; Saarinen, Bajasaari, Backman and Siimes, 1979).



6.16. *Protective properties of human milk.* Among the anti-infective components of human milk are included lactoferrin, immunoglobulins, bifidus factor and living cells (Goldman and Smith, 1973; Hanson, Carlsson, Ahlstedt, Svanborg and Kaisser, 1975; Hanson, 1976; Robinson, Harvey and Soothill, 1978; McClelland, McGrath and Samson, 1978). Artificial foods for young infants and human milk which have been processed by heat treatment are more or less deficient in respect of these components.

6.17. *Upper and lower limits for the amount of protein in infant feeds.* In spite of the uncertainties discussed in paras 6.11–6.14, a minimum amount of 1.5 g of whole cows' milk protein (Total N x 6.38)/100 ml of reconstituted feed would provide sufficient of the total sulphur-containing and all other essential amino acids for the healthy young infant (Table 6.4) even if the casein:whey ratio has not been modified. A maximum concentration of 2.0 g protein/100 ml of reconstituted feed is permissible and would not be too great a contribution to the renal osmolar load.

6.18. If the casein:whey ratio were adjusted to be the same as that of human milk a lower limit of 1.2 g/100 ml for the amount of protein could be considered. Some artificial foods in which this modification has been made are already available. There should be careful scrutiny of any such formulation, since the composition of the whey protein in cows' and human milk is different and not all the whey nitrogen in human milk is available as a source of amino acids.

6.19. The energy content of a reconstituted feed has already been recommended (para 5.11) as 65–75 kcal (270–315 kJ)/100 ml. The range of the percentage of available energy derived from protein would therefore be from 8 per cent (from a reconstituted feed which yields 75 kcal/100 ml and contains 1.5 g protein/100 ml) to 12 per cent (from a feed which yields 65 kcal/100 ml and contains 2 g protein/100 ml). These ranges of energy and protein concentration permit the production of an infant formula in which the percentage of energy derived from protein is somewhat greater than that yielded on average by human milk.

6.20. *Protein quality.* The proteins of infant formulae should supply approximately the same pattern and amounts of amino acids as those of human milk. To ensure that this will be so, it is necessary not only to determine the amino acid composition of the formula but also to carry out appropriate biological assays or laboratory tests to confirm that no significant loss of protein quality has occurred either during the manufacturing process or during storage for the normal shelf life of the product.

#### 6.21. *Recommendations*

We recommend that the amount of protein (total N x 6.38) in any food for the young infant in which the casein:whey ratio is that found in cows' milk should ensure at least 1.5 g and not more than 2.0 g/100 ml of reconstituted feed.



6.22. We agree that the amount of protein can be less than 1.5 g/100 ml of reconstituted feed if the casein: whey ratio is adjusted to be closer to that characteristic of human milk. A lower limit of 1.2 g/100 ml feed is suggested.

6.23. We further recommend that the protein quality should be assessed by reference to the amino acid composition of human milk and by appropriate biological assays or laboratory tests.

## 7. Carbohydrate

7.1. *The carbohydrate of human and cows' milk* is predominantly lactose. Human milk contains on average about 7.4 g carbohydrate/100 ml and cows' milk contains about 4.8 g/100 ml (expressed as the monosaccharide or as lactose monohydrate — see footnote para 5.1) (Table 1). Lactose contributes about 40 per cent of the total energy of human milk and about 26 per cent of the total energy of cows' milk. Human milk contains small amounts of oligosaccharides of the lactose series, the importance of which is not known.

7.2. *Nutritional considerations.* On hydrolysis lactose yields an equimolar mixture of galactose and glucose. It is doubtful whether lactose can be regarded as an essential nutrient. Galactose, which is necessary for the synthesis of some glycolipids, glycoaminoglycans and glycoproteins of the central nervous system, can be synthesized from glucose in the liver. Moreover, some children receive diets which are free of galactose and lactose for years in the treatment of either galactosaemia or lactose intolerance without obvious ill effects (Donnell, Collado and Koch, 1961).

7.3. Lactose is associated with stool acidity and an intestinal flora which may be important in suppressing the growth of *Escherichia coli* in the intestine of breast-fed infants (Bullen and Willis, 1971). Animal studies have shown that, in preference to other carbohydrates, lactose may increase the absorption of calcium, magnesium and strontium (Vaughan and Filer, 1960). Studies in infants however have either not confirmed these reports or given conflicting results.

7.4. Most of the lactose in human milk is digested and absorbed, but too great an intake of lactose can cause diarrhoea. The stools of breast fed infants, who may ingest as much as 10 g lactose/kg bodyweight/day, often contain a small amount of reducing sugars (Southgate and Barrett, 1966). However, there is considerable variation between infants. Fosbrooke and Wharton (1975) found in their study of low birthweight infants who were receiving daily intakes of lactose up to 20 g/kg bodyweight that, although 30 per cent of the infants did have frequent stools, the remainder thrived. Infants accept more carbohydrate in the feed than is present in human milk provided that the extra amount is not all lactose.



7.5. The carbohydrates lactose, sucrose, glucose, maltodextrins and corn syrup have all been used in the manufacture of infant formulae (Widdowson, 1973; Fomon, 1974; Widdowson, Southgate and Schutz, 1974; Mettler, 1976). Starch is not digested by the young infant because there is little pancreatic  $\alpha$ -amylase activity (Miller and Holzel, 1974), but sucrose, dextrins, maltose and lactose are all digested by intestinal sucrase, maltase and lactase (Auricchio, Rubino and Murset, 1965). There is, however, a limit to the amount of lactose which can be tolerated by the young infant (para 7.4).

7.6. A theoretical concern that the use of sucrose might lead to obesity or hyperlipidaemia was not substantiated in the study of low birthweight infants by Fosbrooke and Wharton (1975). Over a period of 3 months, the infants who were given an artificial milk to which sucrose had been added were thinner and their plasma triglyceride concentrations were lower than those of infants who were fed a milk which contained added lactose.

7.7. *Upper and lower limits for the amount of lactose in infant feeds.* Feeds for healthy young infants should contain lactose and it would be inadvisable to depart too far from the composition of human milk with respect to this carbohydrate. The maximum concentration of lactose (expressed as monosaccharide) should approximate to the upper limit of the range found in average human milk (Table 1), that is to say 8 g/100 ml.

7.8. Although infants can be given artificial feeds based on whole cows' milk which contains only about 4.8 g lactose/100 ml apparently without ill effect, there is little evidence upon which to base a minimum concentration for lactose. Infant formulae in which carbohydrates other than lactose are added to cows' milk appear to be as satisfactory as those in which lactose has been added. The amount of lactose in such formulae may be as little as 2.5 g/100 ml feed and this is accepted as the lower limit for the amount of lactose.

7.9. *Upper and lower limits for the total amount of carbohydrate in infant feeds.* A figure of 10 g total carbohydrate/100 ml feed is suggested as an upper guideline.

7.10. The total amount of carbohydrate in an infant feed should provide not less than the amount in cows' milk, that is to say, 4.8 g (expressed as monosaccharide)/100 ml reconstituted feed.

7.11. *Nature of added carbohydrate.* Permitted carbohydrates should be limited to those known to be digested and absorbed without any harm. There is no evidence that the carbohydrates at present in use (lactose, glucose, maltose, maltodextrins and sucrose) are in any way harmful to the young infant but infant formulae containing substantial amounts of carbohydrates other than these should be especially evaluated.



### 7.12. *Recommendations*

We recommend that the total amount of carbohydrate in any infant feed should be not more than 10.0 g and not less than 4.8 g (both expressed as monosaccharide)/100 ml of reconstituted feed.

7.13. We also recommend that the concentration of lactose expressed as monosaccharide should be not more than 8.0 g/100 ml reconstituted feed and not less than 2.5 g/100 ml of reconstituted feed.

7.14. We further recommend that any carbohydrate which is added in the manufacture of infant formulae must be one that has been shown to be digested and absorbed and to cause no harm.

## 8. Fat

8.1. *Fat in human and cows' milk.* The concentrations of fat in human and in cows' milk are approximately the same. The fat consists mainly of triglycerides but also contains phospholipids and sterols. Macy and Kelly (1961) give 3.8 g fat/100 ml as the average for mature human milk with a range of 3.6–4.7 g/100 ml. Fomon (1974) quotes the fat in human milk as 4.5 g/100 ml and recent analyses of pooled samples of human milk give an average fat concentration of about 4.2 g/100 ml (Table 1). The figure 4.2 g/100 ml is comparable with a mean value of 4.03 g/100 ml (range 3.51–4.83 g/100 ml) found by Southgate and Barrett (1966) in a study in which all the milk was collected throughout 72 hours from 10 women (Southgate, personal communication 1976). There is a diurnal variation in the fat content of human milk, the amount being least in the early hours of the morning (Gunther and Stanier, 1949). There is also a variation within any one feed, the 'hind' milk being richer in fat than the 'fore' milk (Young, 1961; Hytten, 1954). The fat content of commercially bulked raw cows' milk is about 3.8 g/100 ml (Kon, 1972; Federation of United Kingdom Milk Marketing Boards, 1978).

8.2. Although there is some variation in the fatty acid composition of milk, the pattern of the triglycerides is different in human and cows' milk (Table 8.1). Human milk contains no butyric acid and a smaller proportion of the other short and medium chain saturated fatty acids than cows' milk. In both milks palmitic acid is the most abundant saturated fatty acid.

8.3. Human milk is richer in the mono-unsaturated fatty acids (chiefly oleic acid) and in polyunsaturated fatty acids. Linoleic (18 : 2, n-6) and possibly  $\alpha$ -linolenic (18 : 3, n-3) are 'essential' fatty acids because they cannot be synthesized in the animal body. Linoleic and  $\alpha$ -linolenic acids are not interconvertible and linoleic acid is present in far greater quantity than  $\alpha$ -linolenic acid in human milk. Both acids can be metabolized to form longer chain polyunsaturated fatty acids which belong either to the linoleic (n-6) or to the linolenic (n-3) series. These derivatives, for example arachidonic acid (20 : 4, n-6) and

**Table 8.1:** Typical amounts<sup>1</sup> of the different fatty acids in mature human and cows' milk expressed as g/100 g total fatty acid and as mg/100 ml milk.

Fatty acid		Fatty acids as g/100 g total fatty acids		Fatty acids as mg/100 ml milk <sup>2</sup>	
		Human Milk	Cows' Milk	Human Milk	Cows' Milk
Butyric	4:0	0	3.2	0	118
Caproic	6:0	0	2.0	0	74
Caprylic	8:0	Tr	1.2	Tr	44
Capric	10:0	1.4	2.8	54	103
Lauric	12:0	5.4	3.5	213	129
Myristic	14:0	7.3	11.2	290	413
Palmitic	16:0	26.5	26.0	1051	959
Stearic	18:0	9.5	11.2	393	413
Others		Tr	2.1	Tr	77
<b>Total saturated</b>		<b>50.1</b>	<b>63.2</b>	<b>2001</b>	<b>2330</b>
Myristoleic	14:1	Tr	1.4	Tr	52
Palmitoleic	16:1	4.0	2.7	160	100
Oleic	18:1	35.4	27.8	1408	1026
Others		1.1	1.8	44	66
<b>Total mono-unsaturated</b>		<b>40.5</b>	<b>33.7</b>	<b>1612</b>	<b>1244</b>
Linoleic	18:2	7.2	1.4	285	52
Linolenic	18:3	0.8	1.5	32	55
Arachidonic	20:4	Tr	Tr	Tr	Tr
Others		Tr	Tr	Tr	Tr
<b>Total poly-unsaturated</b>		<b>8.0</b>	<b>2.9</b>	<b>317</b>	<b>107</b>

Source: Department of Health and Social Security, 1977  
Paul and Southgate, 1978

<sup>1</sup>Considerable variations occur in the amounts of fatty acids in milk.

<sup>2</sup>Calculated on the assumption that 1 g milk fat contains 0.945 g fatty acids.

Tr = trace

docosahexaenoic acid (22 : 6, n-3) are found as traces but in greater amounts in human milk than in cows' milk.

8.4. The composition of milk fat is influenced by the quality and the quantity of fat in the mother's diet. Insull, Hirsch, James and Ahrens (1959) and Kramer, Szoke, Lindner and Tarjan (1965) showed that, when energy intake was adequate, the fatty acid composition of milk fat resembled that of dietary fat. This was not so, however, when the energy intake was inadequate.

8.5. Table 8.2 shows the linoleic acid content of the fat of human milk, as a percentage of total fatty acids, from women in different populations. Percentages as low as 1.0 per cent and as high as 15.2 per cent have been reported. The women with the highest proportion were refugees living in Jordan and were having a diet rich in linoleic acid (Read, Lutz and Tashjian, 1965). African mothers from the lake region of Tanzania, whose customary diet was rich in carbohydrate and low in fat, had the lowest proportion of linoleic acid and the highest proportion of medium chain fatty acids in their milk (Read, Lutz and Tashjian, 1965).



**Table 8.2:** *The amount of linoleic acid (C18:2) in the fat of breast milk from women of different populations (expressed as g/100 g of the total fatty acids)*

Country or population	per cent linoleic acid	Reference
Tanzania	1.0 <sup>1</sup>	Read, Lutz and Tashjian (1965)
Bedouin	6.3	Read, Lutz and Tashjian (1965)
U.S.A.	6.4	Insull, Hirsch, James and Ahrens (1959)
Pakistan	7.0	Underwood, Hepner and Abdullah, (1970)
Italy	7.1	Bonvini, Brughera and Cantone (1967)
U.K.	7.2	Department of Health and Social Security (1977)
U.K.	8.2	Crawford, Hall, Laurance and Munhambo (1976)
Hungary	8.9	Kramer, Szoke, Lindner and Tarjan (1965)
Uganda	9.7	Crawford, Hall, Laurance and Munhambo (1976)
Tanzania	10.0	Crawford, Hall, Laurance and Munhambo (1976)
Lebanon	11.3	Read, Lutz and Tashjian (1965)
Denmark	12.0	Crawford, Hall, Laurance and Munhambo (1976)
Tanzania	12.4	Boersma (1979)
U.S.A.	14.4	Guthrie, Picciano and Sheehe (1977)
Nigeria	15.1	Naismith (1973)
Jordan	15.2	Read, Lutz and Tashjian (1965)

<sup>1</sup>see para. 8.5

8.6. *Nutritional considerations — absorption of fat.* Milk fat is an important source of energy and of the fat soluble vitamins. At one week old a breast-fed infant absorbs more than 90 per cent of the ingested fat, whereas an infant of the same age absorbs only about 70 per cent of the fat in cows' milk (Widdowson, 1965). Young breast-fed infants also absorb fat better than those who are given feeds in which the fat of cows' milk has been partly or completely replaced by other animal fats and vegetable oils in order to simulate the fatty acid pattern of human milk (Southgate, Widdowson, Smits, Cooke, Walker and Mathers, 1969; Hanna, Navarrete and Hsu, 1970), and the fat from such feeds is better absorbed than the fat of cows' milk (Williams, Rose, Morrow, Sloan and Barnes, 1970). Absorption of fat in infancy depends partly on the fatty acid composition of the fat. Shorter chain fatty acids are better absorbed than longer chain acids, and unsaturated fatty acids are better absorbed than saturated fatty acids of the same chain length (Holt, Tidwell, Kirk, Cross and Neale, 1935; Barltrop and Oppé, 1973; Barltrop, 1974). Absorption of fat also depends on the configuration of the triglycerides. Pancreatic lipase releases fatty acids in the 1 and 3 positions, but not in the 2 position; free fatty acids originally in the 1 and 3 positions are therefore available for absorption along with monoglycerides in the 2 position. Palmitic acid is quantitatively the most important long chain saturated fatty acid in human and cows' milk fat (Table 8.1). In human milk fat 72 per cent of the palmitic acid is in the 2-position of the



triglyceride molecule; in cows' milk fat 39 per cent of the palmitic acid is in the this position. There is evidence that 2-monopalmitin is more easily absorbed than free palmitic acid and this may be another reason why infants absorb more of the fat of human milk than of cows' milk (Tomarelli, Meyer, Weaver and Bernhart, 1968; Filer, Mattson and Fomon, 1969; Rey and Ricour, 1972).

8.7. Besides these qualitative factors that influence the absorption of fat, the quantity of fat is also important. The young infant's capacity to absorb fat is limited and as intake is increased a smaller percentage of it is absorbed until at higher levels of intake any additional increase results in an equal rise in faecal fat. The ability to absorb fat increases as the infant grows older, but breast milk fat is still absorbed better than cows' milk fat, at any rate for the first month or so (Southgate, Widdowson, Smits, Cooke, Walker and Mathers, 1969).

8.8. *Essential fatty acids (EFA)*. The human infant has been shown to have a specific requirement for linoleic acid (Hansen, Haggard, Boelsche, Adam and Wiese, 1958). Infants who were fed experimental milk foods which provided less than 0.1 per cent of the energy from linoleic acid developed a characteristic deficiency syndrome. The main features of this syndrome were an immediate decrease in the concentration of linoleic acid (18:2, n-6) and its derivative arachidonic acid (20:4, n-6) in the plasma, accompanied by an increase in the concentration of another polyunsaturated fatty acid, now known to be eicosatrienoic acid (20:3, n-9), impaired energy utilization, evidenced by a marked rise in voluntary food consumption, which was detected within 1-2 weeks, and dermatosis - the development of a dry, scaly thickened skin - which usually appeared only after many weeks of feeding.

8.9. The presence of eicosatrienoic acid in significant amounts in the tissues is indicative of a low intake of linoleic acid, and a value of 0.4 for the ratio of eicosatrienoic acid to arachidonic acid, the so-called triene:tetraene ratio, is generally accepted as the upper limit of normality (Holman, 1970). There is one description only of naturally occurring linoleic acid deficiency in the literature, in infants suffering from kwashiorkor (Naismith, 1973), but iatrogenic essential fatty acid deficiency in infants fed intravenously with fat-free preparations has been reported (Paulsrud, Pensler, Whitten, Stewart and Holman, 1972).

8.10. Hansen, Haggard, Boelsche, Adam and Wiese (1958) concluded that the minimum requirement for linoleic acid in the diet was 1 per cent of the total energy, although it was stated that clinical symptoms of deficiency had not been described in infants when fed artificial milks which usually provided somewhat less. They further suggested that the optimal intake might well be the amount of linoleic acid in the milk of mothers who ate an average American diet and which provided approximately 4 per cent of the total energy of the milk. In the few subsequent studies in which cows' milk was used, the numbers of subjects were small, the conditions of the experiments and the analytical techniques poorly defined, the tests limited by ethical considerations and the results conflicting (Woodruff, Bailey, Davis, Rogers and Coniglio, 1964; Pikaar and Fernandes, 1966).



8.11. The requirement for linoleic acid has recently been reassessed by Naismith, Deepröse, Supramaniam and Williams (1978), who fed 20 infants for the first 14 weeks of life a milk which contained only cows' milk fat. Mean rates of growth in length and in weight were identical with those of 20 matched breast-fed infants, and voluntary food consumption (kcal/kg/day) showed the normal decline throughout the study. There was no clinical evidence of essential fatty acid deficiency, and in none of the infants did the triene:tetraene ratio in the lipids of the plasma or of the erythrocyte membrane approach 0.4. The artificial food used in the trial provided approximately 0.6 per cent of the energy from linoleic acid. In a similar study in which a cows' milk formula was fed for 4 months, the plasma triene:tetraene ratio was again well below 0.4. (Crawford, Hall, Laurence and Munhambo, 1976). Fosbrooke and Wharton (1975) also failed to detect clinical signs of deficiency in 15 low birthweight infants who were fed for 3 months on artificial feeds based on cows' milk in which linoleic acid provided no more than 0.5 per cent of the energy.

8.12. Two new theories concerning the lipid requirements of the human infant have recently been advanced: that  $\alpha$ -linolenic acid, (18:3, n-3) should also be regarded as an essential fatty acid (Lamprey and Walker, 1976), and that pre-formed long-chain polyunsaturated derivatives of both linoleic and  $\alpha$ -linolenic acid may have a role in infant nutrition (Crawford, Sinclair, Msuya and Munhambo, 1973). However, the latter opinion has been recently revised (Crawford, 1977);  $\alpha$ -linolenic acid (18:3, n-3), like linoleic acid (18:2, n-6), cannot be synthesized by mammalian tissues and  $\alpha$ -linolenic acid cures only some of the symptoms of essential fatty acid deficiency in rats (Greenberg, Clabert, Savage and Deuel, 1950). Long chain polyunsaturated derivatives of both linoleic and  $\alpha$ -linolenic acid occur in relatively large amounts in the lipids of cell membranes. This raises the possibility of a functional requirement for the parent fatty acid of each series.

8.13. The accumulation of long-chain polyunsaturated acids (C20 and above) in the developing brain starts before birth, but it continues afterwards, and myelination is not complete until about four years of age (Dobbing and Sands, 1973). The tissues of the newborn infant are capable of synthesizing these long chain fatty acids from their precursors, linoleic (C18:2) and linolenic acids (C18:3), and the brain appears to have a priority for the precursors when supplies are short. Studies with young rats have shown that diets low in linoleic acid and linolenic acids caused no significant alteration to the composition of the phosphoglycerides in the brain (Svennerholm, Alling, Bruce, Karlsson and Sapia, 1972). However, an increase in the ratio of linoleic to linolenic acid in the diet caused a significant increase in docosapentaenoic acid (C22:5) and decrease in docosahexaenoic acid (C22:6) in the ethanolamine phosphoglycerides of the brains of 21 day old rats, and studies by Pavey (1979) on newborn guinea pigs have confirmed these findings. The young guinea pigs of mothers having 20 per cent maize oil in their diets had significantly more linoleic, arachidonic (C20:4) and docosapentaenoic acids and less docosahexaenoic acid in the phosphatidyl ethanolamine and phosphatidyl choline fractions of cerebrum, cerebellum and brain stem than the young of mothers having



the stock diet with or without additional beef fats. There is no proof, as yet, that the lipids of the infant's brain would be altered by feeding a milk containing a fat rich in linoleic acid, but the results of the animal experiments suggest that this cannot be ruled out.

8.14. *Fats and oils used in the manufacture of infant formulae.* Fats and oils from a variety of animal and vegetable sources are being used in the manufacture of infant formulae. There is no evidence that the fat mixtures used at present have adverse effects, but there is some doubt about the use of hydrogenated fats and oils. Naturally occurring polyunsaturated fatty acids are of the *cis* configuration but on partial hydrogenation fatty acids containing double bonds of the *trans* configuration are produced. In the rat, some of the *trans* isomers have been shown to be incorporated in the structural lipids of cells, and to depress the formation of the longer chain derivatives of linoleic and linolenic acids (Kummerow, 1974). As yet, opinion is divided as to the significance of these findings. The triglycerides in human milk contain unsaturated fatty acids of which a small proportion (approximately 10 per cent) have the *trans* configuration (Aitchison, Dunkley, Canolty and Smith, 1977).

8.15. *Cholesterol.* The cholesterol content of human and cows' milk is approximately the same (Table 1). Darmady, Fosbrooke and Lloyd (1972) found that the concentration of cholesterol in the serum of a young infant depended on the type of milk fed. The concentration was greater in breast-fed infants than in those having cows' milk fat. Widdowson, Dauncey, Gairdner, Jonxis and Pelikan-Filipkova (1975) found that serum cholesterol concentration in infants was lower still when the fat of cows' milk was replaced by maize oil. A reduction in the concentration of cholesterol in maternal serum which was induced by increasing the intake of vegetable oils has been shown not to affect the concentration of cholesterol in the milk. However, the resulting increase in the amount of linoleate in milk led to a decrease in the concentration of cholesterol in infant serum (Potter and Nestel, 1976). There is no evidence that the amount of dietary cholesterol or polyunsaturated fat given to young infants is related to serum cholesterol concentration or to the development of atherosclerosis in later life. (Glueck, Tsang, Balistreri and Fallat, 1972; Lloyd, 1976).

8.16. *Upper and lower limits for the total amount of fat in infant feeds.* Guidelines for the upper and lower limits of the energy content and for the amounts of protein and carbohydrate in an infant feed have already been set. Calculations based on these guidelines indicate that limits for the fat content of a feed could be from about 2.3 to 5.0 g fat/100 ml feed (Appendix 1, Table 4). The concentration of fat should not be very different from that in human milk and fat mixtures should contain amounts of stearic, palmitic and oleic acids which approximate to the amounts in human milk from well-nourished mothers.

8.17. *Upper and lower limits for the amount of polyunsaturated fatty acids in infant feeds.* There is no evidence that the relatively low intake of polyunsatu-



rated fatty acids which used to be provided by infant foods based on full-cream cows' milk was in any way harmful to the physical and mental health of the infant. An artificial feed should not provide less than 0.5 per cent of the total energy from linoleic acid (para 8.12). Although a specific requirement for  $\alpha$ -linolenic acid has yet to be demonstrated, the presence of this fatty acid is known to exert a sparing effect on linoleic acid. It is nevertheless suggested that a milk providing as little linoleic acid as 0.5 per cent total energy should contain a similar amount of  $\alpha$ -linolenic acid, that is to say, the total amount of these two polyunsaturated fatty acids should provide at least 1 per cent of the total energy.

8.18. The need for an upper limit to the concentration of polyunsaturated fatty acids is considered. In the study by Widdowson, Dauncey, Gairdner, Jonxis and Pelikan-Filipkova, (1975) there was a rapid increase in the amount of linoleic acid in the adipose tissue of infants who were given feeds in which the fat contained 60 per cent of the fatty acids as linoleic acid, whereas the amount of linoleic acid in adipose tissue of infants who were given feeds containing unaltered cows' milk fat remained the same as at birth. Although all the infants thrived and the proportion of linoleic acid in adipose tissue decreased when the milk with a high polyunsaturated fat content ceased to be fed, further research is needed to establish whether or not the temporary change in adipose tissue composition is in any way harmful. Studies have shown that the change is accompanied by alterations in the phospholipid composition of cell membranes in animals (Pavey, Widdowson, and Robinson, 1976) and of at least the red cell membrane in infants (Farquhar and Ahrens, 1963). A large intake of linoleic acid may suppress the formation of the longer chain derivatives of  $\alpha$ -linolenic acid and may also lead to a relative vitamin E deficiency (para 9.2.3.4).

8.19. For the present therefore we are uncertain about an upper limit for polyunsaturated fatty acids and think it prudent to allow a concentration not greatly in excess of that found in human milk. Although about 16 per cent of the total fatty acids would be in keeping with the maximum linoleic acid content of human milk (Table 8.2) there is no evidence to suggest that harm would result if the upper limit were 20 per cent.

#### 8.20. *Recommendations*

We recommend that the amount of fat in an infant feed should be not less than 2.3 g and not more than 5.0 g/100 ml reconstituted feed.

8.21. We recommend that the linoleic and  $\alpha$ -linolenic acid content of any infant feed should together provide at least 1 per cent of the total energy and that linoleic acid should provide not more than 20 per cent of the total fatty acids.

8.22. We recommend that, before any infant formula is approved, or any substantial change is made in the fat composition of a product, it is advisable that appropriate trials and fat balance studies should be made.



## 9. Vitamins

### 9.1. General considerations

9.1.1. In the United Kingdom clinical evidence of vitamin deficiency or excess in young infants, either breast-fed or artificially fed, is very uncommon. Vitamins are necessary to the infant but little is known about their passage across the placenta, their role in fetal growth or the needs of the newborn for dietary sources of vitamins in addition to tissue stores. Elucidation of these areas of ignorance may place guidelines for the vitamin content of infant feeds on a firmer scientific basis in the future. Meanwhile it seems reasonable to ensure that the concentrations of vitamins in infant feeds should approximate to those in human milk although the amounts of the various vitamins in the maternal diet may influence the concentrations of them in milk (Kon and Mawson, 1950).

9.1.2. There can be a loss of vitamin activity in infant formulae either during the manufacturing process or on storage. To compensate for such losses, an excess (overage) of the vitamin(s) may be added. There is no evidence that intakes in excess of physiological requirements are harmful with the exception of vitamins A, D and K. There is also no evidence that intakes of vitamins in excess of physiological requirements are beneficial. Claims that additional vitamins convey some advantage are deprecated. The problems of shelf life and overages are the responsibility of the manufacturer (see footnote to para 4.3) and a tolerance may be required for all recommended maxima.

### 9.2. Fat soluble vitamins

#### 9.2.1. Vitamin A

9.2.1.1. *Vitamin A in human and cows' milk.* Retinol is the main contributor to the vitamin A activity of milk although cows' milk and some human milks also contain the retinol precursor  $\beta$ -carotene. Human colostrum has about twice as much vitamin A activity as mature human milk (Macy, 1949). The concentration of vitamin A in human milk depends on the maternal diet, and very wide variations in individual samples have been reported (Macy and Kelly, 1961). Recent analyses of human milk gave a value of 60  $\mu\text{g}$  retinol/100 ml with a range of 40–76  $\mu\text{g}$ /100 ml for five pooled samples (Table 2). Cows' colostrum also has a high vitamin A activity. There is a marked seasonal variation in the vitamin A activity of cows' milk. Mean values for retinol and  $\beta$ -carotene were 31 (winter-summer range, 27–36) and 17 (winter-summer range, 12–21)  $\mu\text{g}$ /100 ml respectively (Thompson, Henry and Kon, 1964).

9.2.1.2. *Nutritional considerations.* Vitamin A is essential for growth, for normal vision in dim light and for maintaining the integrity of epithelial cells. Retinol is stored in the liver and is mobilized from that organ in combination with a retinol-binding protein. Vitamin A deficiency is characterized, both in childhood and in adult life, by impaired dark adaptation leading to blindness



associated with xerophthalmia. Signs of deficiency are rare in the developed countries although in some developing countries vitamin A deficiency is a common cause of blindness.

9.2.1.3. Overdosage of vitamin A with medicinal preparations can cause signs of toxicity (Caffey, 1950) but large intakes, for example of at least 5500  $\mu\text{g}$  retinol in aqueous suspension/day for a minimum of 6 weeks, must be consumed before harmful effects are apparent (Persson, Tunnel and Ekegren, 1965). Much larger doses of non-aqueous solution have been given without toxic symptoms appearing (Kramer, Sobel and Gottfried, 1947).

9.2.1.4. *Upper and lower limits for the amount of vitamin A in infant foods.* Vitamin A deficiency is unknown in breast-fed infants in the United Kingdom. Rodrigues and Irwin (1972) found that 10  $\mu\text{g}$  retinol/kg body weight/day was adequate for normal weight gain and for dark adaptation. Fomon (1974) suggested twice this amount as an advisable intake in the young infant. If the minimum intake of milk by the young infant is accepted as being rarely less than 120 ml/kg body weight/day (Fomon, Thomas, Filer, Ziegler and Leonard, 1971), then the minimum concentration of vitamin A, by inference, should be 8.5  $\mu\text{g}/100$  ml feed. However we suggest that the minimum concentration in any artificial feed should be equal to the least amount found in pooled human milk (Department of Health and Social Security, 1977), that is to say, 40  $\mu\text{g}/100$  ml feed.

9.2.1.5. Because an excessive intake of retinol can be toxic, an upper limit to the amount in any infant feed must be set. Toxicity occurs only with persistently high intakes (para 9.2.1.3) As much as 300  $\mu\text{g}$  retinol/100 ml feed would not cause harm even allowing for the fact that the infant may be receiving a vitamin supplement. This would allow the manufacturer to add sufficient overage but 150  $\mu\text{g}$  retinol/100 ml feed should be regarded as the upper limit of the guideline.

9.2.1.6. *Recommendation.*

We recommend that any infant formula should contain not less than 40  $\mu\text{g}$  and not more than 150  $\mu\text{g}$  retinol equivalent/100 ml reconstituted feed.

9.2.2. *Vitamin D*

9.2.2.1. *Vitamin D in human and cows' milk.* Harris and Bunker (1939) were among the first to measure the vitamin D activity of human milk and their single analysis of a composite sample of breast milk gave a result of 0.41 i.u. or 0.01  $\mu\text{g}$  vitamin D/100 ml. This value was quoted by Macy and Kelly (1961). McCance and Widdowson (1967) used the figure 0.026  $\mu\text{g}/100$  ml and Fomon (1974) gave the value of 0.055  $\mu\text{g}/100$  ml human milk. Le Boulch, Gulat-Marnay and Raoul (1974) estimated vitamin D<sub>3</sub> (cholecalciferol) in the lipid fraction of breast milk and obtained a value of 0.18  $\mu\text{g}/100$  ml. Thompson, Henry and Kon (1964) found United Kingdom cows' milk to contain 0.02  $\mu\text{g}$  vitamin D/100 ml.



9.2.2.2. Japanese and French workers (Sahashi, Suzuki, Higaki and Asano, 1967, 1969; Le Boulch, Gulat-Marnay and Raoul, 1974) have reported that both human and cows' milk contain a water soluble conjugate of vitamin D in the form of vitamin D sulphate which has a similar biological activity for rats to that of ergocalciferol (vitamin D<sub>2</sub>). Analyses by Lakdawala and Widdowson (1977) have confirmed the presence of vitamin D sulphate in milk from healthy mothers (Table 9.1). If the biological activity of vitamin D sulphate in human milk proves to be similar to that of fat soluble vitamin D, a breast fed infant would on average receive 0.9 µg biologically active vitamin D sulphate/100 ml milk in addition to the small amount of the fat soluble vitamin. Together these provide about the same concentration of vitamin D as is in fortified infant feeds when they are reconstituted according to the manufacturers' instructions (Department of Health and Social Security, 1974).

**Table 9.1:** Concentration of vitamin D sulphate in human and cows' milk

	Stage of Lactation Days	Number of samples	Vitamin D sulphate mean ± S.D. µg/100 ml
Human milk	3 – 5	18	1.78 ± 0.39
	6 – 8	11	1.00 ± 0.29
	29 – 42	19	0.91 ± 0.40
Cows' milk (pasteurized)		Pooled sample	0.15

Source: Lakdawala and Widdowson (1977)

9.2.2.3. *Nutritional considerations.* Vitamin D is essential for growth, is important in the absorption of calcium and in deposition of calcium salts in the collagenous matrix of developing bone. Deficiency may contribute to neonatal tetany and poor mineralization of bones and teeth. In growing infants rickets is caused by deficiency of vitamin D.

9.2.2.4. Vitamin D occurs naturally in animal fats as cholecalciferol (vitamin D<sub>3</sub>). Ergocalciferol (vitamin D<sub>2</sub>) can be produced by ultra-violet irradiation of plant sterols. Vitamin D<sub>3</sub> can be synthesized in the body by the action of sunlight on 7-dehydrocholesterol in the skin, but so far no accurate measurement of the amount of the vitamin synthesized in this way has been made. The principal metabolites of vitamin D in the body are 25-hydroxycholecalciferol formed in the liver and 1,25 dihydroxycholecalciferol in the kidney. Vitamin D is stored in the body, some in the liver and more in adipose tissues (Mawer, Backhouse, Holman, Lumb and Stanbury, 1972). The vitamin D status of the mother affects the amount of the vitamin present in the fetus and in the newborn infant, (Rosen, Roginsky, Nathenson and Finberg, 1974; Hillman and Haddad, 1976). If the mother is deficient in vitamin D the newborn infant is also at risk of hypocalcaemia and tetany (Bakwin, 1937; Watney, Chance, Scott and Thompson, 1971; Purvis, Barrie, Mackay, Wilkinson, Cockburn, Belton and Forfar, 1973; Watney and Rudd, 1974).



9.2.2.5. *Upper and lower limits for the amount of vitamin D in infant feeds.* Infants who are exposed to sufficient bright sunlight have little need for dietary vitamin D but, in the United Kingdom during the winter, conditions are such that there may be little or none synthesised in the skin and there is a greater dependency on vitamin D in the feed. The provision of an adequate amount in infant feeds is necessary. Lack of quantitative knowledge about the synthesis of vitamin D<sub>3</sub> in the skin precludes any exact statement about requirements for the vitamin.

9.2.2.6. Too great an intake, of the order of 3750 µg per day of vitamin D, can be harmful (British Pharmaceutical Codex, 1973). Signs of toxicity include a failure to thrive and the abnormal deposition of calcium in the body tissues. Intakes have to be large, more than 250 µg vitamin D/kg bodyweight/day, before these signs appear. However, cases of idiopathic hypercalcaemia were reported in the 1950s (Lightwood, 1952) when fortification of infant foods was such that an infant might receive 100 µg per day (British Paediatric Association, 1956; Ministry of Health and Department of Health for Scotland, 1957).

9.2.2.7. If the least volume of milk consumed by a younger infant weighing 8 kg were 120 ml/kg body weight/day (Fomon, Thomas, Filer, Ziegler and Leonard 1971) a concentration of 1.0 µg vitamin D/100 ml feed would provide a total daily intake of 10 µg. Infant milks which are at present available provide this amount of vitamin D.

#### 9.2.2.8. *Recommendations.*

We recommend that any infant feed should provide about 1.0 µg vitamin D (40 i.u.)/100 ml reconstituted feed and we accept the range 0.7–1.3 µg vitamin D/100 ml feed.

9.2.2.9. We recommend that the vitamin be added as ergocalciferol (vitamin D<sub>2</sub>) or cholecalciferol (vitamin D<sub>3</sub>).

### 9.2.3. *Vitamin E*

9.2.3.1. *Vitamin E in human and cows' milk.* Vitamin E is the name given to a group of fat soluble tocopherols which are antioxidants; α-tocopherol has the greatest biological activity, is the most abundant in milk and is contained in many other foods. The analyses of pooled samples of human milk indicated an average concentration of α-tocopherol of 0.35 mg/100 ml with a variation of 0.29–0.39 mg/100 ml (Table 2). The value given by Fomon (1974) is 0.18 mg/100 ml. The average concentration of vitamin E in cows' milk was found to be 0.09 mg/100 ml and, as with other fat soluble vitamins, there is a seasonal variation in the amount of the vitamin (Thompson, Henry and Kon, 1964).

9.2.3.2. Using the values for vitamin E quoted in Table 2 and for fatty acids in Table 8.1 the ratio of vitamin E to polyunsaturated fatty acid (as linoleic acid) in pooled samples of human milk was calculated to be 1.1 mg vitamin E: 1 g linoleic acid, and in cows' milk 0.84 mg vitamin E: 1 g linoleic acid.



9.2.3.3. *Nutritional considerations.* Vitamin E acts with selenium to promote and maintain the stability of biological membranes (Diplock, 1974). Vitamin E deficiency is not common in healthy infants born at term or in young children but has been described (Khurshid, Lee, Peake and Bloom, 1975) and is characterized by enhanced platelet function (Lake, Stuart and Oski 1977). Clinical evidence of deficiency is almost entirely restricted to premature infants who became anaemic when given artificial feeds which had an increased content of polyunsaturated fatty acids relative to the vitamin E content (Oski and Barness, 1967; Ritchie, Fish, McMasters and Grossman, 1968). Newborn infants have low blood concentrations of vitamin E (McWhirter, 1975; Petrich, von Voss, Lietke and Göbel, 1976), and blood from these infants shows, *in vitro*, a decreased stability of red cell membranes in the presence of oxidizing agents. Thus the red blood cells of an infant who is deficient in vitamin E would, during *in vitro* tests, be more readily haemolysed. This fact may be relevant to the occurrence of haemolytic anaemia in some infants who are born pre-term. Administration of  $\alpha$ -tocopherol restores the stability of the erythrocyte membrane (Lo, Frank and Hitzig, 1973).

9.2.3.4. Williams, Shott, O'Neal and Oski (1975) have shown, *in vitro*, that the stability of the red cell membrane is related to the ratio of the plasma concentrations of antioxidant (vitamin E) to polyunsaturated fatty acids rather than to an absolute amount of vitamin E. Thus the infant's requirement for vitamin E should be defined in relation to the amount of polyunsaturated fatty acids.

9.2.3.5. *Upper and lower limits for the amount of vitamin E in infant feeds.* The concentration of  $\alpha$ -tocopherol in plasma appears to be satisfactory from the point of view of haemolysis if the amounts of vitamin E and linoleic acid in the feed are in the ratio of at least 0.4 mg vitamin E: 1 g polyunsaturated fatty acids (Lewis, 1969). A ratio of 0.6 mg vitamin E: 1 g polyunsaturated fatty acids was recommended by Witting (1972).

9.2.3.6. The only evidence of harm if the intake of vitamin E is too high is reported to be an interference with wound healing (Ehrlich, Tarver and Hunt, 1972; Dallman, 1974). We therefore advise some caution in the amount of vitamin E contained in infant feeds but there is insufficient evidence for an upper limit to be recommended with any confidence. The amount of vitamin E should be not less than that in human milk, and the ratio of vitamin E to polyunsaturated fatty acids should be at least 0.4 mg vitamin E: 1 g polyunsaturated fatty acids.

9.2.3.7. *Recommendations.*

We recommend that the amount of  $\alpha$ -tocopherol should be such as to ensure that the ratio of  $\alpha$ -tocopherol (mg) to polyunsaturated fatty acids (g) is at least 0.4:1.0.

9.2.3.8. We recommend that an infant feed should contain not less than 0.3 mg  $\alpha$ -tocopherol/100 ml of reconstituted feed, that is to say, the amount found on average in mature human milk.



#### 9.2.4. Vitamin K

9.2.4.1. *Vitamin K in human and cows' milk.* Very few determinations have been made of the vitamin K content of milk, but the available results show that human milk contains less than cows' milk. Human milk contains about 1.5  $\mu\text{g}/100\text{ ml}$  (Dam, Dyggve, Larsen and Plum, 1952) whereas cows' milk contains about 6  $\mu\text{g}/100\text{ ml}$  (Dam, Dyggve, Larsen and Plum, 1952; Goldman and Deposito, 1966). The reported range in cows' milk was 1.0 to 8.5  $\mu\text{g}/100\text{ ml}$  (Schneider, Fluckiger and Manes, 1974).

9.2.4.2. *Nutritional considerations.* Vitamin K is a generic description which includes the fat-soluble methylnaphthoquinone derivatives that are necessary for the normal clotting of blood. Vitamin K<sub>1</sub> (phylloquinone or phytomenadione) occurs in green plants and vitamin K<sub>2</sub> (other menaquinones) are synthesized by the microbial flora of the gut. Vitamin K<sub>3</sub>, synthetic menaphthone, has been shown to be absorbed from the colon of newborn infants (Aballi, Howard and Triplett, 1966), but whether this finding is applicable to other forms of vitamin K is not fully established (Keenan, Jewett, and Glueck, 1971).

9.2.4.3. Signs of deficiency, other than within the early neonatal period, have not been reported in either healthy bottle-fed or breast-fed infants.

9.2.4.4. *Upper and lower limits for the amount of vitamin K in infant feeds.* It is routine paediatric practice in many maternity hospitals to give a single dose of vitamin K<sub>1</sub> (phylloquinone) to infants immediately after birth. Thereafter the amount in human milk and the present artificial feeds appears to be adequate.

#### 9.2.4.5. Recommendation

We suggest that an infant feed should contain not less than 1.5  $\mu\text{g}/100\text{ ml}$  vitamin K.

### 9.3. Water soluble vitamins

#### 9.3.1. Vitamins of the B complex

9.3.1.1. *B Vitamins in human and cows' milk.* Table 2 sets out the results of the recent analyses of samples of human milk (Department of Health and Social Security, 1977), together with the average values for the concentrations in cows' milk. Except for nicotinic acid, there are more of all the vitamins of the B complex in cows' milk than in human milk. Nicotinic acid can be formed in the body from tryptophan and so further amounts of this vitamin may be produced in infants who are given foods which supply more tryptophan than is needed for protein synthesis.

9.3.1.2. *Nutritional considerations.* The vitamins to be considered are thiamin (B<sub>1</sub>), riboflavin (B<sub>2</sub>), nicotinic acid and nicotinamide (niacin), vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, folic acid, pantothenic acid and biotin. Little is known about the infant's stores of these vitamins except vitamin B<sub>12</sub>.



9.3.1.3. Deficiency diseases can be caused by an inadequate intake of the individual vitamins, but the clinical picture varies according to which vitamin is deficient and whether the body lacks one or more of these vitamins at the same time. Disease caused by a lack of the B vitamins is extremely rare both in breast-fed and bottle-fed infants. An exception occurred when convulsions in bottle-fed infants were found to be due to a deficiency of vitamin B<sub>6</sub> because there were unexpected losses of the natural vitamin B<sub>6</sub> during manufacture (Coursin, 1954).

9.3.1.4. The requirements for both thiamin and riboflavin are related to energy intake and the requirement for vitamin B<sub>6</sub> is related to protein metabolism. For none of the B vitamins are infant requirements precisely known but by inference amounts provided by human milk must be sufficient.

9.3.1.5. *Upper and lower limits for the amounts of B vitamins in infant feeds.* The lower limit of the concentration of any B vitamin in an artificial feed should not be less than in human milk. The concentration of these vitamins in milk has been shown to depend on dietary intake (Kon and Mawson, 1950). The values given in Table 2 are mean values and ranges for pooled samples of human milk. A wider range of values would be obtained if individual samples were analysed. Amounts less than those recommended would not necessarily be harmful.

9.3.1.6. The toxicity of all the B vitamins is low and no toxic symptoms have been demonstrated. Any intake of these vitamins in excess of that required for tissue saturation is of no benefit to the infant and is excreted via the kidney. No upper limit is set for the amounts of B vitamins in artificial feeds.

9.3.1.7. *Recommendations.*

We recommend that foods for the young infant should contain vitamins of the B complex/100 ml of reconstituted feed in amounts not less than the lower limit of the range in pooled samples of human milk (Appendix 1, Table 2).

	μg	minimum
thiamin	μg	13
riboflavin	μg	30
nicotinic acid/nicotinamide	μg	230
vitamin B <sub>6</sub>	μg	5
vitamin B <sub>12</sub>	μg	0.01
folic acid	μg	3
pantothenic acid	μg	200
biotin	μg	0.5

9.3.2. *Vitamin C*

9.3.2.1. *Vitamin C in human and cows' milk.* The amount of vitamin C in human milk has been shown by workers in a number of different countries to vary with the season of the year and with the dietary intake of the mother (Kon and Mawson, 1950). Analysis of pooled samples of human milk (Table 2) showed an average value for the vitamin C concentration (ascorbic acid +



dehydroascorbic acid) of 3.8 mg/100 ml with a range in the 5 pooled samples of 3.1–4.5 mg/100 ml. This mean value is lower than the 4.3 mg/100 ml previously quoted by Fomon (1974) and much lower than the 6.4 mg/100 ml of Macy and Kelly (1961). Fresh cows' milk contains about 2 mg vitamin C/100 ml (Table 2).

9.3.2.2. *Nutritional considerations.* Vitamin C is a powerful reducing agent and is easily and reversibly oxidized to dehydroascorbic acid which is very sensitive to heat. Both the reduced and oxidized forms of ascorbic acid are biologically active and occur in foods including milks.

9.3.2.3. Deficiency is manifested by the disease scurvy. The vitamin is actively transferred by the placenta so that the vitamin C concentration in fetal blood is substantially higher than that in the maternal blood. Clinical scurvy occurs very rarely in breast-fed infants.

9.3.2.4. *Upper and lower limits for the amount of vitamin C in infant feeds.* No symptoms of toxicity have been reported as a result of a high intake of vitamin C. As far as is known, any excess over requirements is metabolized and the breakdown products are excreted in the urine. The amount present in human milk appears to be adequate for the young infant, and therefore the amount of ascorbic acid should be not less than 3.0 mg/100 ml feed. No upper limit for the amount of vitamin C in feeds is suggested. Present knowledge has not as yet shown any advantage in amounts greater than those in human milk.

9.3.2.5. *Recommendation*

We recommend that infant feeds should provide a minimum of 3.0 mg ascorbic acid/100 ml reconstituted feed.

## 10. Sodium, Potassium, Chloride, Calcium, Phosphorus and Magnesium

### 10.1. General

10.1.1. Many inorganic nutrients are known to be essential for man. Of these, sodium, potassium, chloride, calcium, phosphorus, and magnesium are present in the human body and in milk in relatively large amounts and are therefore considered separately from the trace elements.

### 10.2. Sodium, potassium and chloride

10.2.1. *Concentration of sodium, potassium and chloride in human and cows' milk.* Mature human milk contains about 15 mg sodium, 60 mg potassium and 43 mg chloride/100 ml with a range of means for five pooled samples of 11–20 mg sodium, 57–62 mg potassium and 35–55 mg chloride (Table 3). Cows' milk contains about 50 mg sodium (range 35–90 mg), 150 mg potassium (range 110–170 mg) and 95 mg chloride (range 90–110 mg)/100 ml (Table 3).



10.2.2. *Nutritional considerations.* It seems likely that nearly all the sodium, potassium and chloride in milk is absorbed, although much of what is absorbed is not retained. Dietary deficiencies of these nutrients are unlikely to occur. Any deficiencies are caused by excessive losses from the body as in severe diarrhoea. Clinical problems may also arise if there is an excessive intake of these nutrients, particularly of sodium.

10.2.3. As far as is known, in the first few months of life the kidney of the young infant can excrete an excess of potassium ions (Tudvad, McNamara and Barnett, 1954) and this seems also to be true for an excess of chloride. For about the first 10–14 days after birth the kidney of the young infant, compared with that of the adult, re-absorbs sodium ions from the glomerular filtrate more efficiently and also has a limited capacity to excrete water. An increased intake of sodium therefore leads to over-hydration and hypertonicity (McCance and Widdowson, 1957; Thodenius, 1974). Although potassium and chloride ions are more readily excreted than sodium, an obligatory amount of water is needed for their excretion, and too great an intake of potassium and chloride may affect the volume and composition of body fluids.

10.2.4. Any increase in renal solute load may be of relatively little significance in most circumstances because the kidney can compensate by excreting a more concentrated urine but there is a decreased margin of safety against dehydration. For example, if the intake of water is reduced or there is an increased loss of water from the lungs, skin or gut due to infection or high ambient temperature, the young kidney may be unable to increase the urine concentration sufficiently, and this may contribute to hypertonic dehydration (Pratt and Snyderman, 1953; Ziegler and Fomon, 1971). In this country hypertonic dehydration can be a complication of infant diarrhoea and the mortality rate is usually greater than from hypotonic or isotonic dehydration (Macaulay and Blackhall, 1961; Morris-Jones, Houston and Evans, 1967; Ironside, Tuxford and Heyworth, 1970; Banister, Matin-Siddiqi and Hatcher, 1975; Tripp, Wilmers and Wharton, 1977). Furthermore, serious neurological sequelae occur in some of the survivors (Macaulay and Watson, 1967). A recent apparent decline in the incidence of hypertonic dehydration and hypernatraemia as a complication of gastroenteritis has been attributed to the increased use of feeds which have a protein and mineral content approximately that of human milk (Pullan, Dellagrammatikas and Steiner, 1977; Sunderland and Emery, 1979; Arneil and Chin, 1979). Other workers, however, have reported a similar decline even when the less modified feeds continued to be in common use (Whalley and Walker-Smith, 1977; Tripp, Wilmers, and Wharton, 1977).

10.2.5. Some concern has been expressed about the possible rôle of a high sodium intake in the development of hypertension. There is experimental evidence from animal studies that high salt intakes in early life can result in hypertension later (Dahl, 1972). Epidemiological evidence of a relationship between salt intake and a raised blood pressure in man, is, as yet, inconclusive (Freis, 1976).



10.2.6. *Upper and lower limits for the amounts of sodium, potassium and chloride in infant feeds.* A healthy infant receives adequate amounts of sodium, potassium and chloride if breast-fed and therefore the lower limits for the concentrations of these nutrients in infant feeds should correspond to those in mature human milk.

10.2.7. In order to lessen the adverse effects of an increased renal solute load the upper limits for these nutrients should be less than the concentration found in whole cows' milk. Only by a process of demineralisation can a sodium concentration close to that of average mature human milk be achieved. Although demineralized formulae have been used for some time without harm, demineralization, at least in theory, may remove nutrients at present unidentified. Upper limits for sodium, potassium and chloride cannot be precisely defined with any degree of accuracy, but acceptable limits can be derived empirically by a consideration of values which obtain when cows' milk is diluted to the protein content already recommended, and by consideration of experience with milks at present available in the United Kingdom.

10.2.8. The upper limit for the amount of protein in infant milk foods has already been set at 2.0 g/100 ml of reconstituted feed (para 6.21). In order to achieve this protein concentration and to maintain the energy value of the feed at about 70 kcal/100 ml (para 5.11) by the addition of carbohydrate the mineral concentration of cows' milk is reduced so that the concentration of sodium is about 35 mg, of potassium about 90 mg, and of chloride about 60 mg/100 ml of reconstituted feed. These amounts could be considered as upper limits but the mineral content of cows' milk varies with the time of year and changes in animal feed. We therefore recommend the following limits (para 10.2.9) in the knowledge that potassium and chloride are readily excreted by the infant kidney, and that the limits set for sodium in infant feeds are also compatible with normal function of the healthy infant kidney.

#### 10.2.9. *Recommendations*

We recommend that an infant feed should contain not less than 15 mg sodium, 50 mg potassium and 40 mg chloride per 100 ml of reconstituted feed, and not more than 35 mg sodium, 100 mg potassium and 80 mg chloride per 100 ml of feed. In SI units these values correspond to not less than 6.5 mmol sodium, 13 mmol potassium and 11 mmol chloride, and not more than 15 mmol sodium, 26 mmol potassium and 23 mmol chloride per litre of reconstituted feed.

### 10.3. **Calcium, phosphorus and the calcium:phosphorus ratio**

10.3.1. *Concentration of calcium and phosphorus in human milk.* Mature human milk contains about 35 mg calcium and 15 mg phosphorus/100 ml with a range of means for the five pooled samples of 32–36 mg calcium and 14–15 mg phosphorus/100 ml (Table 3). Cows' milk contains about 120 mg calcium (range 110–130 mg) and 95 mg phosphorus (range 90–100 mg)/100 ml (Table 3).



10.3.2. *Nutritional considerations (a) General.* Calcium and phosphorus have varied and different functions in the body. Combined as hydroxyapatite they form the main mineral constituent of bone and other calcified tissues. The human fetus at term contains about 28 g calcium and 16 g phosphorus (Widdowson and Spray, 1951). Most of the calcium has accumulated during the latter weeks of gestation and is contained in the skeleton, and 2 per cent in the soft tissues where phosphate is the main cellular anion. Calcium ions have an important role in cell function, in determining the excitability of peripheral nerves and muscle and in the clotting of blood. The concentration of calcium in the body fluids is regulated by a complex and incompletely understood mechanism which involves phosphorus, vitamin D, parathyroid hormone and calcitonin. During the first few weeks of life the young infant is less able than the older child or adult to regulate the plasma calcium concentration and hypocalcaemia may result in tetany. This occurred more often in artificially fed infants than in breast-fed infants (Gittleman and Pincus, 1951).

10.3.3. The dietary intake of calcium and phosphorus should be adequate to meet the needs of the rapidly growing skeleton in order that normal calcification can proceed. In addition it is important that the balance of these minerals available from the diet should be such that the young infant is able to regulate the concentrations of calcium and phosphorus in the body fluids.

10.3.4. (b) *Absorption of calcium and phosphorus.* It is difficult to measure true calcium absorption in young infants because a significant fraction of the faecal calcium is derived from gut secretions (Sutton and Barltrop, 1973). Net absorption, that is to say the difference between food and faecal calcium can, however, be measured and there is little doubt that calcium is better absorbed by the human infant from human milk than from cows' milk (Fomon, Owen, Jensen and Thomas, 1963). This difference may be related to the amount and nature of the fatty acids present in the milk fat (Southgate, Widdowson, Smits, Cooke, Walker and Mathers, 1969). The ratio of calcium to phosphorus in milk is also important, as has been shown in breast-fed infants by Widdowson, McCance, Harrison and Sutton (1963), and in artificially fed infants by Barltrop, Mole and Sutton (1977). Other nutrients may affect calcium absorption, for example lactose (para 7.3), which improves absorption in animals (Lengemann, Wasserman and Comar, 1959; Patrick and Stirling, 1973). Phosphorus is absorbed more readily than calcium and is much less affected by the presence of other substances in the intestine.

10.3.5. Large intakes of calcium and phosphorus may increase the requirement for magnesium in animals (Morris and O'Dell, 1963) and lead to hypomagnesaemia, and large intakes of magnesium are associated with increased calcium absorption (Seelig, 1971).

10.3.6. (c) *Metabolism of calcium and phosphorus.* It is perhaps surprising that the mineral content of cows' milk should be conducive to hypocalcaemia and neonatal tetany. Bakwin in 1937 suggested that it was the greater phosphate concentration rather than the calcium concentration which was the



predominant factor. Oppé and Redstone (1968) and Barltrop and Oppé (1970) showed that healthy infants who were fed unmodified cows' milk products had a significantly greater concentration of phosphorus and smaller concentration of calcium on the sixth day of life than breast-fed infants or those fed on modified milks. Determination of the plasma calcium and phosphorus on the 6th day has been used in several subsequent investigations designed to show deviations from normal calcium homeostasis in the newborn (Lealman, Logan, Hutchison, Kerr, Fulton and Brown, 1976; Belton, Cockburn, Forfar, Giles, Kirkwood, Smith, Thistlethwaite, Turner and Wilkinson, 1977). These confirm the physiological advantages of using infant feeds in which the concentrations of inorganic constituents are similar to those in human milk.

10.3.7. Purvis, Barrie, Mackay, Wilkinson, Cockburn, Belton and Forfar (1973) showed also that neonatal hypocalcaemia was associated with maternal deficiency of vitamin D. This and other evidence indicates that disorders of calcium metabolism in the neonatal period have many causes apart from imbalances in the mineral composition of the infant's diet. Although neonatal tetany is the most obvious clinical manifestation of hypocalcaemia there are other important associations, such as dental hypoplasia reported by Stimmler, Snodgrass and Jaffe (1973). For a healthy infant born at term the requirement for calcium and phosphorus is met most adequately and safely by a feed which does not differ markedly in mineral composition from that of human milk.

10.3.8. *Upper and lower limits for the amounts of calcium and phosphorus in infant feeds.* Since there is evidence of harm from too much phosphate but not from an increased calcium concentration in milk it seems reasonable to set an upper limit for phosphate which is unlikely to cause hyperphosphataemia and we suggest that 100 ml of reconstituted feed should contain no more than 60 mg of phosphorus. An upper limit for the calcium concentration is less easy to define because the efficiency with which calcium is absorbed from a given feed is selectively regulated and is dependent on the other nutrients present. Provided that calcium in an infant feed is as readily absorbed as from human or cows' milk, a concentration of 120 mg/100 ml, that is to say, the concentration found in cows' milk, is a reasonable upper limit.

10.3.9. Deficiencies in the dietary intake of calcium and phosphate could in the short term be met by the mobilization of these minerals from the skeleton, but the infant's diet should include sufficient to promote normal mineralization of the growing bone. Neonatal hypocalcaemia is a dangerous condition, which is not generally related to deficient calcium intake although too large an intake of phosphorus is a contributory factor. There is no reason to depart from the concentrations of calcium and phosphorus found in average mature human milk and therefore the lower limits can be set at 30 and 15 mg/100 ml feed respectively.

10.3.10. The absorption and metabolism of calcium and phosphorus are closely related. There is evidence of harm when the ratio of calcium to phosphorus is reduced compared with that in human milk and optimal plasma



calcium concentration occurs when the calcium phosphorus ratio found in human milk is maintained (Barltrop and Oppé, 1970; Barltrop, Mole and Sutton, 1977). The calcium:phosphorus ratio should not be less than that of cows' milk (1.2:1) or greater than that in human milk (2.2:1).

10.3.11. The absorption of calcium from milk is affected by the presence of other nutrients (para 10.3.4). It is possible that an artificial feed could contain amounts of calcium and phosphorus which are within the suggested limits and with an acceptable calcium to phosphorus ratio but which nevertheless would result in inadequate calcium absorption or an unacceptable disturbance of calcium homeostasis. Appropriate evaluation of infant feeds is therefore important in respect of these minerals.

#### 10.3.12. *Recommendations*

We recommend that the concentration of calcium in a feed should be not less than 30 mg and not more than 120 mg/100 ml, and that of phosphorus be not less than 15 mg and not more than 60 mg/100 ml of reconstituted feed.

10.3.13. We recommend that the ratio of calcium to phosphorus be not less than 1.2:1 as in whole cows' milk and not more than 2.2:1 as in human milk.

### 10.4. Magnesium

10.4.1. *Magnesium in human and cows' milk.* Human milk contains about 2.8 mg magnesium/100 ml with a range for the means of pooled samples of 2.6–3.0 mg/100 ml, and cows' milk contains about 12 mg magnesium/100 ml with a range of 9–14 mg (Table 3).

10.4.2. *Nutritional considerations.* The body of the newborn healthy infant contains about 750 mg of magnesium (Widdowson and Spray, 1951) of which a large part is in bone. In the soft tissues it is mainly bound to protein and is, next to potassium, the predominating cation of the cells. It is an essential part of many enzyme systems responsible for the transfer of energy.

10.4.3. Although cows' milk has a larger concentration of magnesium than human milk, hypomagnesaemia may result from feeding unmodified cows' milk to infants because of the phosphate content (Anast, 1964; Coussons, 1969). Hypocalcaemia is usually accompanied by a decrease in the concentration of serum magnesium, particularly when the calcium concentration is reduced enough to cause the convulsions of neonatal tetany (Tsang, 1972; Cockburn, Brown, Belton and Forfar, 1973; Caddell, 1974). Although an increase in calcium intake may have no effect on the plasma magnesium concentration, the low blood calcium and magnesium may both be restored to normal values when the magnesium intake is increased (Fomon, 1974). Wilkinson (1973) and Cockburn, Brown, Belton and Forfar (1973) have found that in some cases the convulsions can be allayed only by giving magnesium.



10.4.4. Seelig (1971) has suggested that, providing the minimum mineral requirements of an infant are met, an increased magnesium intake results in an increase in calcium retention (para 10.3.5). Widdowson, McCance, Harrison and Sutton (1963) found that in the newborn breast fed infant the absorption of magnesium was increased when supplementary phosphorus was given.

10.4.5. Hypermagnesaemia has been reported in the young infant following the use of magnesium sulphate in pregnancy and can result in neuromuscular dysfunction which may take four or five days to return to normal (Lipsitz, 1971; Tsang, 1972).

10.4.6. *Upper and lower limits for the amount of magnesium in infant feeds.* The amount of magnesium in an infant feed should at least be that found in mature human milk. There is no evidence to suggest that harm results from the higher concentration of magnesium in cows' milk *per se* but an infant feed should not contain more magnesium than is found on average in cows' milk.

#### 10.4.7. *Recommendations*

We recommend that in any infant feed the amount of magnesium should be such as to provide not less than 2.8 mg and not more than 12 mg/100 ml of reconstituted feed.

## 11. Iron

11.1. *Concentration of iron in human and cows' milk.* Mature human milk contains about 76  $\mu\text{g}$  iron/100 ml with a range of means for five pooled samples of 62–93  $\mu\text{g}$ /100 ml; cows' milk contains about 50  $\mu\text{g}$  iron/100 ml with a range of 30–60  $\mu\text{g}$ /100 ml (Table 3). Some of the iron in human milk is bound to lactoferrin which is one of the whey proteins.

11.2. *Nutritional considerations.* An infant at term has about 300 mg of iron in its body, of which approximately 15 per cent is present as storage iron in the liver, and most of the remainder is in the blood combined in the pigment haemoglobin of the red cells (Widdowson and Spray, 1951). Iron is also an essential component of cytochrome and flavoprotein enzymes in cells and of muscle myoglobin. Iron is transported in the serum by the iron-binding protein transferrin and is stored in the reticuloendothelial system combined with protein as ferritin. There is little or no haemosiderin present in the young infant.

11.3. Assessment of iron status is difficult because the relationships between the various iron fractions in the body are not fully understood. Iron deficiency is associated with an anaemia which is generally characterized by hypochromia and microcytosis, though the indices used in the adult may not be applicable to the young infant. Biochemical evidence of iron deficiency is sought by estimation of the serum iron concentration and the total iron binding capacity (transferrin concentration) of the blood. Measurement of the concentration of ferri-



tin in the serum has been claimed to provide a sensitive index of the amount of iron stored and a concentration of 8 ng per ml or less is held to indicate iron depletion (Rios, Lipschitz, Cook and Smith, 1975).

11.4. Maintenance of a satisfactory iron status during infancy depends on the amount of iron in the body at birth, the growth rate, and the balance between iron lost from the body and that taken in and absorbed from the diet. There is considerable variation in the amount of iron in the body of the new-born. This is accounted for by differences in body weight and in blood lost or gained from the placenta rather than by maternal iron status (Rios, Lipschitz, Cook and Smith, 1975) although there is some small additional effect due to gestational age (Scott, Berger, Kenward, Scott and Wharton, 1975). The concentration of haemoglobin in the blood just after birth is of the order of 16-20 g/100 ml. The iron contained in this (a little over 200 mg) together with the store of iron in the liver (40-50 mg) and the amount absorbed from breast milk should be sufficient for the infant while birthweight is doubled, particularly as a physiological decrease in haemoglobin concentration to about 10 g/100 ml usually occurs.

11.5. There is evidence that healthy breast-fed infants maintain satisfactory iron status (McMillan, Landaw and Oski, 1976) and the amount of iron in human milk appears to be sufficient as the sole source of exogenous iron. It cannot however be assumed that intakes of similar amounts would be adequate for infants who are artificially fed. Little direct information is available regarding iron absorption and utilization from milk in infancy although it seems clear that the ingestion of unheated, unmodified cows' milk is associated not only with poor iron absorption (Underwood, 1971) but also with microcytic anaemia (Woodruff, Wright and Wright, 1972) and with a tendency to iron loss due to occult gastrointestinal bleeding (Wilson, Lahey and Heiner, 1974). Healthy breast fed infants absorb and utilize iron more efficiently than those who are fed the present modified artificial feeds (Woodruff, Latham and McDavid, 1977; Saarinen, Siimes and Dallman, 1977; Saarinen and Siimes, 1978). Several factors are probably involved in the preferential iron absorption from human milk. These include the form in which the iron is present and the concentrations of other nutrients such as protein, copper and zinc (Gross, 1968).

11.6. Because of uncertainty regarding the availability of iron from foods for the young infant it has become general practice for manufacturers to supplement their products with an iron salt, such as for example ferric ammonium citrate, which is known to be effective (Theur, Martin, Wallender and Sarett, 1973). The American Academy of Pediatrics Committee on Nutrition (1976) recommended that all infant formulae should contain iron in amounts found in human milk but some have iron added greatly in excess of this. A justification for this practice rests on the argument that augmentation of iron stores during the first months of life is a safeguard against the later development of iron deficiency when mixed feeding or cows' milk feeding may provide inadequate amounts of dietary iron (Pearson, 1971). There is however some doubt as to whether or not the gut of an infant absorbs iron in excess of immediate



requirement or whether, as Van Campen (1974) suggests, iron absorption increases as the need for iron increases. There is also evidence in the low birthweight infant that haemolytic anaemia may be precipitated by fortification with iron if there is a relative vitamin E deficiency and high intake of polyunsaturated fatty acids (Williams, Shott, O'Neil and Oski, 1975).

11.7. Lactoferrin, an iron-binding protein, is present at a concentration of about 1.6 g/l in human milk but there is less than 0.2 g/l in cows' milk. Growth of bacteria, for example staphylococci and *Escherichia coli*, are inhibited in vitro by lactoferrin (Reiter and Oram, 1967; Bullen, Rogers and Leigh, 1972) because lactoferrin deprives the bacteria of iron. Addition of iron in amounts sufficient to saturate the lactoferrin may thus facilitate bacterial growth. Equally, destruction of lactoferrin by heat will release iron and so allow bacterial multiplication. Pearson (1971) has pointed out that, although the use of iron-fortified formulae had tripled in the United States of America in five years, a corresponding increase in neonatal infection had not been recognized. Baltimore, Vecchitto and Pearson (1978) have shown that the growth of *Escherichia coli* in commercially available infant formulae was not influenced by the concentration of iron.

11.8. The exogenous iron intake of infants can be increased not only by the use of foods fortified with iron salts but also by the administration of medicinal iron compounds. The latter cannot be recommended as a routine because there is no good evidence that it is effective or beneficial and adverse side effects, although of a minor nature, are not infrequent (Burman, 1972; Fuerth, 1972).

11.9. It is clear that further information is needed about the absorption and efficiency of utilization of the various iron compounds which are commonly added to infant formulae, and about whether the larger amount of iron is beneficial or even necessary. Until there is better understanding of the iron requirements during infancy, it is difficult to propose meaningful guidelines.

11.10. *Upper and lower limits for the amount of iron in infant feeds.* The lower limit for the amount of available iron should be the amount on average in pooled mature human milk, that is to say, 76  $\mu\text{g}$  iron/100 ml of reconstituted feed but iron in human milk is better absorbed by infants than iron from cows' milk or artificial feeds. We understand the arguments against enrichment with larger amounts of iron, but are wary of contravening established practice since there is insufficient evidence to attribute harm to the present foods which contain amounts greater than in either human or cows' milk. However we see no reason for the amount of iron to exceed about ten times the amount in human milk.

#### 11.11. *Recommendation*

We recommend that a reconstituted infant feed should contain not less than 70  $\mu\text{g}$  iron/100 ml and not more than 700  $\mu\text{g}$ /100 ml.



## 12. Trace elements

### 12.1. Introduction

12.1.1. Trace elements are found in milk in lower concentration than the inorganic nutrients discussed in chapter 10 of this report. Not all the trace elements have as yet been shown to be of biological significance to man. Of those which are known to be essential in nutrition (National Academy of Sciences, 1974) the following will be discussed in so far as the information from recent research permits — copper, zinc, manganese, chromium, molybdenum, cobalt, selenium, iodine and fluorine. Little is known about the requirements of the young infant for these nutrients, or about the amounts present in human milk and in infant formulae, or about the factors affecting absorption and metabolism. Even less is known about the significance of the other trace elements which may prove essential in human nutrition (Schwarz, 1971). However recent studies of sick and very low birthweight infants who require parenteral nutrition have provided some quantitative indication of requirements for trace elements and have revealed the signs and symptoms of clinical states caused by deficiency (Karpel and Peden 1972; Sivasubramanian and Henkin, 1978). The results of these investigations cannot be directly applied to the healthy infant but do provide evidence of the need for infant formulae to contain these nutrients.

12.1.2. Table 12.1 summarizes the concentrations of some trace elements in mature human milk and in cows' milk. The amounts present in milk depend in a varying and largely unknown way on the maternal diet. Most of the trace

**Table 12.1:** *The amounts of iron and some of the trace elements in mature human and cows' milk expressed in  $\mu\text{g/ml}$  milk*

	Human milk <sup>1</sup>		Cows' milk	
	Mean	Range for pooled samples	Mean	Range
Iron	70	60 – 90	50 <sup>2</sup>	30 – 60 <sup>2</sup>
Copper	39	37 – 43	20 <sup>2</sup>	10 – 60 <sup>2</sup>
Zinc	290	260 – 330	350 <sup>2</sup>	200 – 600 <sup>2</sup>
Manganese	1.2 <sup>4</sup>	0.7 – 1.5 <sup>5</sup>	3 <sup>3</sup>	—
Chromium	0.6 <sup>5</sup>	—	1 <sup>3</sup>	0.8 – 1.3 <sup>3</sup>
Cobalt	—	—	0.1 <sup>3*</sup>	0.05 – 0.13 <sup>3</sup>
Selenium	1.4	0.8 – 1.9	*	0.5 – 5 <sup>7</sup>
Iodine	7	2 – 12	26 <sup>8*</sup>	—
Fluorine	8	2 – 15	*	3 – 22 <sup>9</sup>

<sup>1</sup>Except where noted otherwise, values from Department of Health and Social Security (1977)

<sup>2</sup>Paul and Southgate (1978)

<sup>3</sup>Underwood (1971)

<sup>4</sup>Cavell and Widdowson (1964), Widdowson (1969)

<sup>5</sup>Broek and Wolff (1935), McLeod and Robinson (1972)

<sup>6</sup>Hambidge (1971)

<sup>7</sup>Hadjimarkos and Bonhorst (1961)

<sup>8</sup>Average value for cows fed on winter rations (Dodd, Kingwill, Shearn, Morant and Lewis, 1975)

<sup>9</sup>Ericsson and Ribelius (1970); McClure (1970); Backer Dirks, Jongeling-Eijndhaven, Flissebaalje and Gedalia (1974).

\*The content in milk varies considerably with the diet of the cow.



elements in milk appear, at least in part, to be bound to protein and perhaps to other molecules. The significance of these 'trace element-protein' complexes is largely unknown. More analyses and research are required.

12.1.3. The nutrients listed above (para 12.1.1) are considered in turn but, although the presence of these nutrients in infant feeds is essential and possible upper and lower limits are discussed, no recommendations as to compositional guidelines are made. Paragraphs 12.11.1 to 12.11.5 make this clear.

## 12.2. Copper

12.2.1. *Copper in human and cows' milk.* Human milk was found to contain about 39  $\mu\text{g}$  copper/100 ml with a range of means for pooled samples of 37–43  $\mu\text{g}$ /100 ml; cows' milk contains about 20  $\mu\text{g}$  (10–60  $\mu\text{g}$ )/100 ml (Table 3). Little is known at present as to whether copper is bound to a whey protein as is the case with iron.

12.2.2. *Nutritional considerations (a) Body stores.* At birth the body of a healthy infant contains about 13.7 mg of copper and more than half of this is stored in the liver (Widdowson and Spray, 1951). Two thirds of the copper in the liver is deposited during the last 8 weeks of gestation (Widdowson, Chan, Harrison and Milner, 1972). This stored copper is gradually withdrawn and is adequate for the demands of growth as well as for the increase in the serum copper concentration which is associated with the maturation of the enzyme system necessary for the synthesis of caeruloplasmin (Cartwright and Win-trobe, 1964; Henkin, Schulman, Schulman and Bronzert, 1973).

12.2.3. (b) *Deficiency.* As far as is known there have been no reports in the United Kingdom of copper deficiency in infants born at term who were either breast fed or given infant formulae not fortified with copper. Copper deficiency has been reported in premature infants who were given milk with a low concentration of copper (Ashkenazi, Levin, Djaldetti, Fishel and Benvenisti, 1973).

12.2.4. (c) *Interaction with other trace elements.* In adult animals copper is known to interfere with the absorption of iron and zinc, and zinc with the absorption of copper (Mills and Williams, 1971). The utilization of copper is also affected adversely by other dietary components. Whether or not these interactions occur in man is not known.

12.2.5. *Upper and lower limits for the amount of copper in infant feeds.* In the absence of any evidence of copper deficiency in healthy infants, there appears to be no nutritional reason for fortification of infant formulae with a copper compound. Nevertheless, some of the formulae marketed at present are so fortified and have been used without apparent harm to infants. It seems likely that the amount of copper in infant feeds should be not more and not less than the amounts present on average in mature human and cows' milk, that is to say, not less than 10  $\mu\text{g}$  and not more than 60  $\mu\text{g}$ /100 ml, but at present sufficient information is not available for a recommendation to be made.



### 12.3. Zinc

12.3.1. *Zinc in human and cows' milk.* Recent analyses give a mean value of about 295  $\mu\text{g}$  (with a range of means for pooled samples of 260–330  $\mu\text{g}$ ) zinc/100 ml of human milk, and a mean of 350  $\mu\text{g}$  (with a range of 200–600  $\mu\text{g}$ ) zinc/100 ml of cows' milk (Table 3). There is a much higher concentration of zinc in colostrum than in mature milk (Berfenstam, 1952).

12.3.2. Nearly 90 per cent of the zinc in cows' milk is bound as a complex to protein (Parkash and Jenness, 1967). A large proportion of the zinc in human milk is bound to low molecular weight proteins (Eckhert, Sloan, Duncan and Hurley, 1977) which differ from the high molecular weight zinc-binding proteins of cows' milk (Evans and Johnson, 1976). This difference may be responsible for the better availability of zinc from human milk than from artificial feeds (Johnson and Evans, 1978). Hurley, Lönnerdal and Stanislawski (1979) give another reason (para 12.3.4).

12.3.3. *Nutritional considerations (a) Body stores.* The body of the full-term fetus contains about 50 mg zinc. The liver has a higher concentration than the body as a whole (Widdowson, Chan, Harrison and Milner, 1972) and contributes about 25 per cent to the total zinc in the body at term. Zinc is also concentrated in hair and male sex organs and it is a constituent of a number of enzymes, including carbonic anhydrase, carboxypeptidase and alkaline phosphatase.

12.3.4. (b) *Deficiency.* Zinc deficiency has been known in man since it was first demonstrated by Prasad, Halsted and Nadimi (1961) but the occurrence of dietary deficiency in the young infant has not been reported. An inherited human zinc deficiency disorder, acrodermatitis enteropathica, has been described (Moynahan, 1974). The symptoms appear only in infants who are not breast fed, and are cured with supplements of zinc. Hurley, Lönnerdal and Stanislawski (1979) have suggested that the beneficial effect of human milk is due to the fact that the zinc in it is bound to citrate, which renders the zinc soluble and easily absorbed. In cows' milk most of the zinc is bound to casein and is consequently less readily absorbed. Healthy breast-fed infants were found to be in negative zinc balance at the end of the first week following birth (Cavell and Widdowson, 1964; Fomon, 1974) and indeed for the first four months infants do not appear to retain sufficient zinc to maintain in the body the concentration of zinc which they had at birth (Fomon, 1974). At what age infants begin to retain zinc and in what quantities have still to be investigated. It has been shown that plasma zinc concentrations of breast fed infants aged six months are not much different from those of adults (Hambidge, Walravens, Casey, Brown and Bender 1979). The concentration of zinc in the hair of infants in the United States of America was found to decline rapidly in the first few months after birth and the concentration found at birth was not regained until about 4 years of age (Hambidge, Hambidge, Jacobs and Baum, 1972). These changes may, however, be physiological rather than a reflection of an inadequate dietary intake.



12.3.5. (c) *Interaction with other trace nutrients.* Interaction of zinc with, for example, copper and cadmium and other dietary constituents has been well documented for animals. Too large an intake of copper has been shown to cause zinc deficiency, and zinc has been shown to counteract some of the adverse effects of cadmium (Underwood, 1971). There is no evidence as yet as to whether these effects can occur in the young infant. The serum cholesterol concentration in animals is said to increase when the dietary ratio of zinc to copper is high (Klevay, 1973). However, Hambidge (1976) was unable to confirm such an increase when the zinc:copper ratio in infants was increased from 5:1 to 17:1.

12.3.6. *Upper and lower limits for the amount of zinc in infant feeds.* There is no information which would suggest that the zinc content of human and cows' milk is insufficient to meet the requirements of the young infant. It is therefore suggested that the concentration of zinc in a reconstituted infant feed should not be below that found in cows' milk ( $200 \mu\text{g}/100 \text{ ml}$ ) and although there is no evidence of harm from a high concentration of zinc in any formula which is at present available, the amount of zinc should not exceed the upper range of values known to occur in cows' milk ( $600 \mu\text{g}/100 \text{ ml}$ ). The concentration of zinc in human milk is between these values.

## 12.4. Manganese

12.4.1. *Manganese in human and cows' milk.* Human milk has a lower concentration of manganese than cows' milk. Broek and Wolff (1935) found  $0.7 \mu\text{g}/100 \text{ ml}$  in mature human milk; Cavell and Widdowson (1964) and Widdowson (1969) found  $1.2 \mu\text{g}/100 \text{ ml}$  and McLeod and Robinson (1972)  $1.5 \mu\text{g}/100 \text{ ml}$  at the end of the first week after birth. The concentration of manganese in colostrum is not very different from that in mature milk (Angelieva and Syarova, 1968). Cows' milk has about  $3 \mu\text{g}$  manganese/ $100 \text{ ml}$  (Underwood, 1971). The concentration varies with the manganese intake of the cow and increases rapidly in response to a dietary supplement.

12.4.2. *Nutritional considerations (a) Body stores.* Little is known about the distribution of manganese in the body of the new-born infant. Widdowson, Chan, Harrison and Milner (1972) found little or no manganese stored in the liver. Manganese is needed for a number of enzyme systems which are involved in oxidative phosphorylation, and in fatty acid and cholesterol synthesis.

12.4.3. (b) *Deficiency.* The liver does not seem to store manganese in the fetus as it does copper and iron. There is some evidence from animal studies that manganese is present in bone at a higher concentration than in other fetal tissues (Gamble, Hansard, Moss, Davis and Lidvall, 1971). Signs of manganese deficiency have not been reported in infants or indeed in older children or adults.

12.4.4. *Upper and lower limits for the amount of manganese in infant feeds.* There is no firm evidence upon which to discuss upper and lower limits for the amount of manganese in infant feeds but the amounts in human milk and in



infant feeds which are at present available appear to be adequate. Thus the manganese content of artificial feeds should be within the range of that found in human milk and in infant formulae which are now available.

## 12.5. Chromium

12.5.1. *Chromium in human and cows' milk.* Hambidge (1971) reported the concentration of chromium to be 1.85  $\mu\text{g}/100\text{ ml}$  in human colostrum and 0.64  $\mu\text{g}/100\text{ ml}$  in mature milk. Underwood (1971) states the amount of chromium in cows' milk to be 1–1.3  $\mu\text{g}/100\text{ ml}$ . Fomon (1974) gives values of 0.8–1.3  $\mu\text{g}/100\text{ ml}$  for cows' milk and does not give a value for human milk. It seems likely that chromium in milk is bound in an organic complex.

12.5.2. *Nutritional considerations (a) Body stores.* Widdowson, Chan, Harrison and Milner (1972) found the concentration of chromium in fetal liver to be variable and not always greater than that in the adult as reported by Tipton (1960).

12.5.3. (b) *Deficiency.* Chromium is regarded as an essential nutrient, and the earliest detectable effect which results from deficiency is an impairment of glucose tolerance (National Academy of Sciences, 1974). Animal experiments suggest that one or more organic chromium complexes behave as a 'glucose tolerance factor', and chromium is transferred across the placenta to the fetus only if present as an organic complex. In the naturally occurring biologically active complex, chromium is bound to nicotinic acid and certain amino acids (Mertz, 1974a).

12.5.4. In children with protein-energy malnutrition, Mertz (1974b) and Gürson and Saner (1973) have shown that supplements of chromium improved glucose tolerance. Turkish infants who were given a chromium supplement gained more weight than infants who were not supplemented (Gürson and Saner, 1973). There have been no reports of chromium deficiency in infants, either breast- or bottle-fed, in the United Kingdom.

12.5.5. *Upper and lower limits for the amount of chromium in feeds.* Present knowledge does not allow any definitive statement as to the amount of chromium that should be present in infant feeds. Some chromium is essential but the addition of chromium salts is not without difficulty because of the possibility of harm since hexavalent chromium salts are toxic.

## 12.6. Molybdenum

12.6.1. *Molybdenum in human and cows' milk.* Published values for the molybdenum content of milk are so variable that it is impossible to state whether species differences exist, or whether there are significant differences in relation to the stages of lactation (Underwood, 1971). The molybdenum content of cows' milk depends on the dietary intake. Thus Archibald (1958)



reported an average of  $7.3 \mu\text{g}/100 \text{ ml}$  which was increased to  $37.1 \mu\text{g}/100 \text{ ml}$  when the cows were given a supplement of ammonium molybdate. Molybdenum in cows' milk is bound as an organic complex in the xanthine oxidase molecule. However, Archibald (1958) found no corresponding increase in the xanthine oxidase of milk when the amount of molybdenum in the milk was increased by feeding a molybdenum supplement. There seems to be no information about the molybdenum content of mature human milk but Oliver, Sperling, Liberman, Frank and de Bres, (1971) found the xanthine oxidase activity of human colostrum to be about one tenth that of cows' milk.

12.6.2. *Nutritional considerations, body stores, deficiency and interaction with other nutrients.* There appears to be no information about the molybdenum content of the infant at birth, and no syndrome of deficiency or of excess has been recognized in infants. Animal experiments show that a low dietary intake of this nutrient affects growth adversely (Reid, Kurnick, Suacha, and Couch, 1956). There is evidence that in the cow an interaction between the absorption of molybdenum and copper occurs, and in non-ruminants a high intake of dietary molybdenum may depress the absorption of copper (Suttle, 1974).

12.6.3. *Upper and lower limits for the amount of molybdenum in infant feeds.* Molybdenum is of importance in relation to enzyme systems but there is no evidence at present upon which to base upper and lower limits for molybdenum in infant feeds other than that the concentration in a reconstituted feed should be within the reported ranges found in cows' milk.

## 12.7. Cobalt

12.7.1. *Cobalt in human and cows' milk.* Archibald (1958) stated that cows' milk contains  $0.1 \mu\text{g}$  cobalt/ $100 \text{ ml}$  with a range  $0.05\text{--}0.13 \mu\text{g}/100 \text{ ml}$ . The few other reported values for the amount of cobalt in human milk do not give consistent results.

12.7.2. *Nutritional considerations.* The concentration of cobalt in the liver does not appear to change during the second half of fetal life and was found to be about  $10\text{--}12 \mu\text{g}/100 \text{ g}$  from 20 weeks gestation to term (Widdowson, Chan, Harrison and Milner, 1972). This was also the concentration found in adult liver. It is considerably larger than that in the whole body of the adult (Forbes, Cooper and Mitchell, 1954; Forbes, Mitchell and Cooper, 1956; Widdowson and Dickerson, 1964). Some of the cobalt in the liver is combined as vitamin  $\text{B}_{12}$  but other protein bound complexes may also exist.

12.7.3. In human nutrition no function has been assigned to cobalt other than its importance as part of the vitamin  $\text{B}_{12}$  molecule. The amount of vitamin  $\text{B}_{12}$  in human milk is not more than  $10 \text{ ng}/100 \text{ ml}$  and, because 4 per cent by weight of vitamin  $\text{B}_{12}$  is cobalt, the amount of cobalt combined as vitamin  $\text{B}_{12}$  in human milk can be calculated to be  $0.4 \text{ ng}/100 \text{ ml}$ . The amount of vitamin  $\text{B}_{12}$  in cows'



milk is 30 ng/100 ml and, by a similar calculation, cows' milk must contain 1.2 ng of cobalt/100 ml as part of vitamin B<sub>12</sub>. This is considerably less than the mean concentration reported by Archibald (1958) (para 12.7.1) and thus, at least in cows' milk, some cobalt is probably present in a form other than vitamin B<sub>12</sub>.

12.7.4. Vitamin B<sub>12</sub> is essential for both man and cow. Man requires a dietary source of the vitamin but the cow does not because microorganisms in the rumen synthesize the vitamin which is then absorbed. Synthesis of vitamin B<sub>12</sub>, but not absorption, occurs in the large intestine in man. In the infant there is a store of vitamin B<sub>12</sub>, and thus of cobalt, in the liver at birth. Human milk and those infant formulae which are at present available appear to provide the amounts of vitamin B<sub>12</sub> and of cobalt which are required by the infant. In high dosage cobalt is toxic.

## 12.8. Selenium

12.8.1. *Selenium in human and cows' milk.* Human milk was found to contain about 1.4 µg selenium/100 ml milk with a range for the means of pooled samples of 0.8–1.9 µg/100 ml (Table 3). In the United States of America, Hadjimarkos (1963) and Hadjimarkos and Shearer (1973) reported 1.3–5 µg/100 ml and Millar and Sheppard (1972) in New Zealand found 1.2–14.5 µg selenium/100 ml mature human milk. Lombeck, Kasperek, Harbisch, Feinendegen and Bremer (1977), working in Germany, obtained values of 1–1.5 µg/100 ml for human milk and 0.7–1.1 µg/ml for cows' milk. The selenium content of cows' milk in the United Kingdom varies greatly and ranges from 0.5–5 µg/100 ml have been reported (Table 3). The concentration depends on the dietary intake. In the USA mean values for cows' milk were 0.5, 4.9 and 6.7 µg selenium/100 ml (Hadjimarkos and Bonhorst, 1961) and in New Zealand, where the selenium content of the soil is low, Grant and Wilson (1968) reported as little as 0.3 µg selenium/100 ml milk.

12.8.2. *Nutritional considerations.* The amount of selenium in the whole body of the newborn infant is unknown. The results of Alexiou, Grimanis, Grimani, Papaevangelou, Koumantakis and Papadatos (1977) suggest that the liver at term contains about 190 µg selenium/100 g. Selenium is an essential part of some enzyme systems, is important for the cell membrane and is closely linked with vitamin E metabolism (Diplock, 1974). There is no evidence of any disease in man which is caused by a deficiency or excess of selenium per se although an excessive intake can be toxic in animals (Moxon and Olson, 1974). There may be some relationship between selenium and the development of the teeth for there was less dental caries in areas of the USA where the soil content of selenium was small compared with where it was larger (Hadjimarkos, 1963; 1969).

12.8.3. *Upper and lower limits for the amount of selenium in infant milk foods.* The amounts in human milk and in infant feeds which are in use at present are presumably adequate. There is no firm evidence upon which to discuss upper



and lower limits for the amount of selenium in artificial feeds, and no recommendation is made.

## 12.9. Iodine

12.9.1. *Iodine in human and cows' milk.* Human milk was found to contain about 7  $\mu\text{g}$  iodine/100 ml with a range for pooled samples of 2–12  $\mu\text{g}$ /100 ml (Table 3). Salter (1950) reported iodine concentrations of 4–8  $\mu\text{g}$ /100 ml in mature human milk. Another reported value is 3  $\mu\text{g}$ /100 ml (Chilean Iodine Educational Bureau, 1952).

12.9.2. Cows' milk was found to have a mean iodine content of 26  $\mu\text{g}$ /100 ml (Table 3) but the content varies considerably with the diet of the cow. It also varies with the time of the year, and concentrations/100 ml have been reported as follows: 4.7  $\mu\text{g}$  (Chilean Iodine Educational Bureau, 1952); 0.97  $\mu\text{g}$  in summer and 2.06  $\mu\text{g}$  in winter in a goitrous region and 2.11  $\mu\text{g}$  in summer and 8.35  $\mu\text{g}$  in winter in a non-goitrous region of Holland (Binnerts, 1954); 1  $\mu\text{g}$  in spring and 20  $\mu\text{g}$  in autumn in Great Britain (Broadhead, Pearson and Wilson, 1965); 6.6  $\mu\text{g}$  in summer to 12.7 in winter on average in Norway (Renaas and Staveland, 1974). The National Institute for Research in Dairying reported values ranging from 1  $\mu\text{g}$ /100 ml milk from a herd in summer without supplementation to 80  $\mu\text{g}$ /100 ml from a herd fed winter rations containing mineral supplements (Dodd, Kingwill, Shearn, Morant and Lewis, 1975); the mean concentration of iodine in winter milk was 32  $\mu\text{g}$ /100 ml milk.

12.9.3. The use of iodophors for teat disinfection increases the amount of iodine in cows' milk. When iodophor teat-dipping (using a solution containing 5000 ppm free iodine) was introduced twice daily after milking in 30 herds on winter rations, the mean concentration in the milk rose from 26  $\mu\text{g}$  to 38  $\mu\text{g}$  iodine/100 ml over a period of 2–3 weeks (Dodd, Kingwill, Shearn, Morant and Lewis, 1975). These workers found that, among grazing cows, the introduction of iodophor teat-dipping led to a mean increase of 27  $\mu\text{g}$  iodine/100 ml within 6 days among cows whose teats were washed with water before each milking, and an increase of 40  $\mu\text{g}$ /100 ml in unwashed cows. Connolly (1971) reported concentrations ranging from 11.2–34.6  $\mu\text{g}$  iodine/100 ml milk from farms where iodophors were used. Iwarsson and Ekman (1974) found that iodine concentrations were increased by a mean value of 17.4  $\mu\text{g}$ /100 ml (range 5.5–35.3  $\mu\text{g}$ ) during periods when iodophor teat-dipping was being used. By contrast, iodophor solution used for the disinfection of milking plant did not add significantly to the amount of iodine in milk.

12.9.4. *Nutritional considerations (a) Body stores.* A large proportion of the iodine in the body is in the thyroid gland. The concentration in the gland is very variable but it increases with age. Most is combined as thyroglobulin, which is the storage compound, but smaller quantities are present as inorganic iodine and mono- and di-iodo tyrosine, and the thyroid hormones thyroxine and tri-iodothyronine. A deficiency of iodine in the diet causes hyperplasia of the thyroid gland and goitre, while a large excess reduces the uptake of iodine by the gland and hence also produces signs of thyroid deficiency.



12.9.5. *Upper and lower limits for the amount of iodine in infant feeds.* Although the amount of iodine in infant feeds should provide not less than the least amount in pooled samples of human milk, that is to say 2  $\mu\text{g}/100\text{ ml}$ , the amount in cows' milk may be as much as 80  $\mu\text{g}/100\text{ ml}$ . There is insufficient information as yet for any compositional guidelines for the iodine content of infant feeds to be recommended.

## 12.10. Fluoride

12.10.1. *Fluoride in human and cows' milk.* Human milk contains about 7.7  $\mu\text{g}$  fluoride/100 ml milk with a range for the means of pooled samples of 2.1–15.5  $\mu\text{g}/100\text{ ml}$  (Table 3). Hodge, Smith and Gedalia (1970) reported values as high as 20  $\mu\text{g}/100\text{ ml}$ . The concentration does not seem to be increased in areas where water is fluoridated (Ericsson and Ribelius, 1970). The amount in cows' milk is similar and ranges from 3–22  $\mu\text{g}/100\text{ ml}$  (Ericsson and Ribelius, 1970; McClure, 1970; Backer Dirks, Jongeling-Eijndhaven, Flissebaalje and Gedalia, 1974).

12.10.2. *Nutritional consideration.* Fluoride accumulates in the hard tissues of the body, the bones and teeth, and this occurs more rapidly in the young growing animal than in the older one. An excessive intake of fluoride causes fluorosis, but a deficiency is associated with dental caries. When the fluoride content of the domestic water supply is low there is a higher incidence of dental caries in developing teeth than in areas where the water contains more fluoride. Epidemiological studies have shown that the consumption of water containing 1 ppm (100  $\mu\text{g}/100\text{ ml}$ ) of fluoride or more reduces the incidence of dental caries by up to 50–60 per cent. A report of the Royal College of Physicians of London (1976) has recommended the fluoridation of water supplies in the United Kingdom to a concentration of 1 ppm. An artificial powdered milk food reconstituted with such water would supply the infant with about 10 times the amount of fluoride that is present in human or cows' milk. There is no evidence that the fluoride which is derived from water used to reconstitute the feed has had any harmful effect in areas where the fluoride concentration is 1 ppm. The work of Ericsson and Ribelius (1970) suggests that there is a considerable margin of safety in the amount of fluoride ingested by the infant.

12.10.3. *Upper and lower limits for the amount of fluoride in infant feeds.* The work of Wiatrowski, Kramer, Osis and Spencer (1975) has shown that the fluoride content of most baby foods and infant formulae is dependent on the fluoride content of water. No recommendation about the fluoride content of artificial milks is made.

## 12.11. Amounts of trace elements in infant feeds

12.11.1. The biological importance of essential trace elements is recognized but so little is known either about requirements for these nutrients (Hambidge, 1976) or about protein-trace nutrient complexes, that compositional



guidelines are not set for all these nutrients. Stores at birth may in some cases, for example copper, be of great importance as a safeguard against a low intake from milk but for others, such as zinc, newborn infants do not have a large store. Human milk and infant formulae should contain sufficient amounts of the trace nutrients. Whatever source of trace elements is used in the manufacture of infant formulae the Scrutiny Panel will wish to have information about the amounts of the different trace elements present in the product.

12.11.2. The process of demineralization, by which the mineral content of cows' milk is reduced, may also decrease the amounts of trace nutrients, cause some change in their complex molecules, or some upset in the 'balance' of these nutrients.

12.11.3. One method of ensuring the presence of trace elements in infant formulae is the addition of 'solids-not-fat' (SNF) of cows' milk as an ingredient. Such an addition would ensure that the trace nutrients are more likely to be present as complex molecules although such complexes derived from cows' milk may not necessarily be identical with the trace nutrient complexes of human milk. Table 12.2 shows the average amounts of SNF which would need to be present in a reconstituted infant feed to provide the concentrations of trace elements which are within the range of those found in human milk.

12.11.4. The amount of any trace nutrient may vary in different samples of milk but, on average, the theoretical maximum amount of SNF that could be present in infant formulae would be 5 g SNF/100 ml feed. This would introduce 1.9 g cows' milk protein which is almost the upper limit of the compositional guidelines for protein. This amount of SNF would also provide on average enough zinc, manganese and iodine but not enough copper or iron to meet the amounts of these nutrients in human and cows' milk and which appear to be adequate for infant feeds. Fluoride and chromium would be present in amounts about the same as those in mature human milk (Table 12.1) Smaller amounts of SNF (1.75g/100 ml feed) have been used in practice and clinical signs of trace element deficiency have not been recognised. Other ingredients used in the manufacture of infant formulae, such as demineralized whey, could also be a source of trace nutrients if, as seems likely, protein-trace nutrient complexes are retained in the process. It should also be remembered that some of the trace nutrients may be introduced into the feed in the domestic water used for reconstitution but the amounts are variable and the extent to which they are biologically available is largely unknown.

12.11.5. In practice most manufacturers in the United Kingdom ensure the presence of trace elements in their products by the addition of SNF from cows' milk whether or not other sources are used. However SNF is not used for some products, and present practice has shown that iodide and some salts of copper, zinc and manganese can be added without evidence of harm.



**Table 12.2:** The contribution made by the addition of different amounts of 'solids-not-fat' (SNF)<sup>1</sup> from cows' milk to the concentration of some trace elements<sup>2</sup> in infant feeds.

	Trace element present in SNF $\mu\text{g}/100\text{ g}$		Minimum of range in pooled samples of human milk $\mu\text{g}/100\text{ ml}$	Suggested possible range/ $100\text{ ml}$ infant feed $\mu\text{g}$	Contribution from 1.75 g SNF / $100\text{ ml}$ feed $\mu\text{g}$	Contribution from 5.0 g SNF / $100\text{ ml}$ feed $\mu\text{g}$	Amount SNF (g/ $100\text{ ml}$ feed) required to provide minimum of range in infant feed	
	Mean	Range					average SNF composition	minimum SNF composition
Iron	562	337-674	60	70-700	10 <sup>3</sup>	28	12	21
Copper	225	112-674	37	10-60	4	11	4	9
Zinc	3933	2247-6742	260	200-600	69	197	5	9
Manganese	34	-	0.7	-	0.6	2	-	-
Chromium	11	9-15	- <sup>3</sup>	-	0.2	0.6	-	-
Cobalt	1	0.6-1.5	-	-	0.02	0.5	-	-
Selenium	-	6-60	0.8	-	0.1 <sup>4</sup>	0.3 <sup>4</sup>	-	-
Iodine	392	-	2	-	7	20	0.5	-
Fluorine	-	34-247	2	-	0.6 <sup>4</sup>	2 <sup>4</sup>	-	23

<sup>1</sup>SNF calculated from Appendix Table 1 as total weight of  $100\text{ ml}$  cows' milk ( $103\text{ g}$ ) minus [water/ $100\text{ ml}$  milk ( $90.2\text{ g}$ ) + fat/ $100\text{ ml}$  milk ( $3.9\text{ g}$ )] =  $8.9\text{ g}/100\text{ ml}$  milk.

<sup>2</sup>Trace elements calculated from Table 12.1.

<sup>3</sup>Average value for human milk  $0.6\ \mu\text{g}/100\text{ ml}$ .

<sup>4</sup>Minimum value.



## 13. Water for reconstitution, renal solutes and acid-base characteristics of feeds

### 13.1. Water

13.1.1. *Water in human and cows' milk.* Both milks contain approximately 90 per cent water (weight/weight).

13.1.2. *Nutritional considerations.* Water is an essential nutrient and is required to replace losses in urine and faeces and from the skin and lungs. A small amount is needed for growth. The infant needs relatively more water than the adult. The chief source of water for the artificially fed infant is that used for the reconstitution of the dried or concentrated liquid manufactured products.

13.1.3. The water most often used for the reconstitution of infant formulae is obtained from the domestic water supply. Domestic water supplies are not of constant composition and vary from one area to another. Variations also occur due to climatic conditions and to changes in the sources of supply. Medical aspects of water quality are under consideration by a Joint Committee of the Department of Health and Social Security and the Department of the Environment. It is recommended practice for tap water to be boiled before it is used in the preparation of infant feeds, and in some instances the main water supply is subjected to a process of artificial softening. Prolonged boiling and artificial softening of water may increase the amounts of some of the dissolved substances, notably the sodium ion, originally present in the water.

13.1.4. *Sodium.* The concentration of sodium is of concern because the overall sodium content of the feed as given to the infant can be markedly influenced by the sodium content of the water used for reconstitution. The upper limit of acceptability for the amount of sodium in a reconstituted feed has been suggested as 35 mg/100 ml (para 10.2.9), that is to say 350 mg or 15 mmol sodium/l, and the lower limit as the amount in average mature human milk, that is to say 15 mg sodium/100 ml or 150 mg (6.5 mmol) sodium/l (para 10.2.7).

13.1.5. Infant formulae which are at present available provide feeds with a sodium content within the range of 15–30 mg sodium/100 ml, that is to say infant formulae contribute 150–300 mg or 6.5–13 mmol sodium/l, to the reconstituted feed. Thus the upper limit guideline for the sodium content of a feed (350 mg/l) could be exceeded, for example, if an infant formula which contributed 300 mg sodium/l were to be reconstituted with water which contained more than 50 mg or 2.2 mmol sodium/l.

### 13.2. Renal solutes

13.2.1. Inorganic ions which are ingested in excess of body requirements or which are produced as metabolic end products together contribute to the renal



solute load. An infant feed which contained the upper limits set for the amounts of protein, sodium, potassium and chloride would result in renal solutes requiring excretion which would not exceed the concentrating power of the infant kidney and would not upset water balance even in a young infant in whom temporary disorders led to moderate degrees of fluid loss. This has been discussed in paras 10.2.6. to 10.2.8.

### **13.3. Acid-base characteristics of feeds**

13.3.1 Human milk has on average a pH of 7.3 with a range of means for pooled samples of mature milk of 6.8–7.7 (Laboratory of the Government Chemist, 1975 personal communication). Definite recommendations as to the suggested range of pH in infant feeds are not made but the pH should not be too much different from the pH of feeds that have been well tried by experience in this country and have been found to be harmless.

13.3.2. Human milk has a higher pH value, less titratable acidity and a smaller buffering capacity than cows' milk. Artificial feeds prepared by reconstitution of infant formulae which are at present marketed have values for pH, titratable acidity and buffering capacity between those for human and cows' milk.

13.3.3. Healthy infants who are given different artificial feeds may have different values for blood pH and other measurements of their acid-base status. Barrie, Martin and Ansell (1975) have suggested that most infant formulae should contain extra alkali, for example sodium bicarbonate or citrate, but Berger, Scott, Kenward, Scott and Wharton (1978) found that the addition provided no clinical advantage.

13.3.4. No recommendation is made but there would be concern if the acid base characteristics of any infant formula were different from those formulae which, by present experience, are considered to be suitable for the young infant.

## **14. Vitamins and mineral salts added during the course of manufacture**

14.1. In sections 9, 10, 11 and 12 of this report, nutritional guidelines have been recommended for the presence of vitamins, inorganic nutrients and trace elements in artificial feeds. To achieve the concentrations suggested, manufacturers may find it necessary in some cases to add vitamins and/or inorganic salts.



14.2. Certain principles which refer to these additions are listed as follows:

- (a) the vitamin or mineral salt should not be a prohibited substance,
- (b) the total amount of any nutrient from all sources should be within the recommended amount of the nutritional guidelines. Tolerance limits may be necessary when there is loss of nutrient during manufacture and storage. Any disadvantageous interaction of added vitamins or mineral salts between each other or with nutrients already present in the milk are taken into account by manufacturers in the calculation of overages. For new products these can be considered in consultation with the Scrutiny Panel.
- (c) the added vitamin or inorganic nutrient should be biologically available.

14.3. Details of added nutrients would have to be supplied before approval could be given to any particular food for the young infant by the Scrutiny Panel.



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### III Other foods which can be used instead of human milk

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#### 15. Foods for the young infant which do not contain any cows' milk protein

15.1. Foods for the young infant which do not contain protein derived from cows' milk may contain either ingredients from the milk of mammals other than the cow or ingredients which are not derived from any milk. At present there are no infant formulae available in the United Kingdom which fall into the first category and it seems unlikely that such foods will be readily available in this country. There are some mothers who, when unable to breast feed, have fed the milk of other mammals, usually the goat, but, unless modified, these milks are unsuitable for young infants.

15.2. Experience in the United Kingdom in the use of foods which contain vegetable sources of protein is limited. Such investigations as have been undertaken have been confined to a limited number of ingredients and chiefly to soya isolates. At present, these foods like many other foods for young infants are not subjected to scrutiny (para 1.1.2). The potential for using a wide range of ingredients in the manufacture of infant formulae is considerable but the more manufacturers use such ingredients the greater the need for vigilance to ensure that the food is in all respects suitable for the young infant. Feeding trials and the careful assessment of results will form an important aspect of the scrutiny of such foods and, for the more novel products, the tests and trials may need to be more exacting and carried out over longer periods of time than was necessary for the foods at present marketed.

15.3. To set an exact specification is even more difficult for these foods. Nevertheless the nutritional guidelines in Part II of this report should in general apply. Some modifications may be needed for the use of other sources of protein than cows' milk protein in order to give due allowance for differences in digestibility, in biological value and in amino acid composition. If and when sufficient knowledge has been gained specific guidelines may then be established.

15.4. Descriptions or names given to these products and whether or not the protein source should be declared are matters which will be considered by the Food Standards Committee.



### 15.5. *Recommendations*

We recommend that foods which do not use cows' milk as a source of protein and which are intended as the sole source of nourishment for the healthy young infant should also be subjected to scrutiny by an expert panel, and that particular emphasis should be given to the need for biological evaluation of these foods.

## 16. Foods for the young infant with special dietary requirements

16.1. In recent years a variety of special infant formulae has been developed for infants who, as a result of abnormal physiological conditions, cannot tolerate human milk or artificial milks used instead of human milk and therefore have special dietary requirements. Special infant formulae may also be necessary for low birthweight infants whose nutritional needs differ from those of the healthy infant born at term. The particular needs of the low birthweight infant are often for only a short period of time and the majority are soon able to transfer to the ordinary infant formulae. The same may not be true for the young infant suffering from abnormal metabolic conditions. Such conditions may persist not only throughout infancy but also into adult life and many of the special formulae which are available are not consumed exclusively by infants.

16.2. Foods for special dietary requirements are generally consumed under medical supervision or on medical advice. In many cases these foods are not suitable as the sole nourishment for the young infant, and either need to be supplemented with vitamins and minerals or form part of a carefully supervised diet. The cost of these foods, due to limited demand and the complexity of their manufacture, is often high. In certain instances the foods may be prescribed as medicines for the treatment of specified conditions such as, for example, phenylketonuria, histidinaemia, tyrosinosis, lactose intolerance and galactosaemia.

16.3. It is clear from the foregoing that foods for infants with special dietary requirements cannot be considered on the same terms as infant formulae for healthy infants. There would be great difficulties in devising all-embracing nutritional guidelines, although the guidelines that have been recommended for infant formulae would not be completely inappropriate.

16.4. Foods for low birthweight infants and infants with special dietary requirements make a significant contribution to the well-being of the less healthy and the present availability and future development of these foods should not be in any way hampered. They are intended to be used only under medical supervision or on the instruction of the medical profession. Nevertheless, if offered for retail sale, these foods should be subjected to the scrutiny we have suggested for milk foods for healthy young infants.



16.5. The ingredients of foods for infants with special dietary requirements should be specified, and both nutrient deficiencies in the food and recommended supplements should be clearly indicated. In addition, such foods should be labelled as 'only to be used on medical advice'.

#### 16.6. *Recommendation*

We recommend that any food marketed as suitable for low birthweight infants, or for infants with special dietary requirements, and which is intended to be used under medical supervision, or on the instructions of the medical profession, should be subjected to scrutiny and to the other controls that have been recommended for infant formulae.



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## IV Non-nutritional aspects of infant feeds

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### 17. Non-nutritional substances in infant feeds

17.1. The Report of the Joint FAO/WHO Expert Committee (FAO/WHO 1972) suggested that "foods intended for infants under 12 weeks should contain no additives at all". The FAO/WHO committee recognized, however, that exceptions to this rule would be necessary. Additives may prevent the deterioration of nutrients or may interact with certain nutrients. The guidelines set for nutrients should not be exceeded as the result of the use of these additives.

17.2. Certain contaminants are present, albeit in minimal amounts, in both human and cows' milk, for example, antibiotic residues, pesticides such as DDT, and radioactive strontium. These and food additives are the concern of the Food Additives and Contaminants Committee (FACC) and of the Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). The two committees are at present reviewing food additives and contaminants in infant milk foods and recommendations about any restrictions are left to them. The FACC has already recommended a further reduction in permitted concentrations of lead in foods which are specially prepared for infants and young children (Statutory Instruments, 1979).

17.3. There will need to be a continuing liaison between on the one hand the FACC and the COT and on the other the Panel set up for the scrutiny of infant milk foods in order to ensure the use of only those additives which are technologically necessary and toxicologically acceptable.

### 18. Reconstitution of infant feeds

18.1. Decisions about the upper and lower limits for the concentration of nutrients in foods for young infants have been made in respect of 100 ml of reconstituted feed and do not allow the addition of any substance other than water. The solute content of the domestic water supply has been discussed (paras 13.1.1 to 13.1.5).

18.2. For convenience of storage and for economic reasons infant formulae are likely to continue to be marketed, as at present, either as dry powders or as concentrated liquids. The products will differ in density and thus the volume of food to be used in reconstituting 100 ml feed will differ from one food to



another. Scoop size may vary from product to product and this may result in errors in the composition of the reconstituted feed either because the wrong scoop has been used or because the correct scoop has been incorrectly filled. The problem and the dangers of under- and over-concentration of feeds have been discussed in an earlier report (Department of Health and Social Security, 1974). Incorrect usage is not always the fault of the person preparing the feed. It is often difficult to avoid the formation of cavities within the powder as the scoop is filled and it is sometimes difficult to get powder out of the bottom of the packet. Instructions as to how to fill the scoop vary with different products. Considerable advantage to the public has been achieved recently by the goodwill of the different manufacturers. The number of scoopsful to be used in the reconstitution of a given volume of feed has been standardized and only the size of the scoop varied to allow for differences in powder density. Interchanging the scoops provided by all but one of the manufacturers would lead to little change in the concentration of reconstituted feeds, so that the chief cause of error in preparing feeds is likely to be an error in counting. One scoopful of product should be added to each 30 ml (or 1 fl oz) of water.

18.3. The dilution of the feed is independent of the age or weight of the infant and instructions about reconstitution can therefore be simple and should also be pictorial. Instructions about the volume of reconstituted feed to be given to infants of different weight should also be simple, and should be accompanied by the information that some individual infants may require more and some less than the average volume for their weight and age.

## 19. Labelling and advertising

19.1. Detailed consideration of the labelling of infant formulae is a matter for the Food Standards Committee but nonetheless there are certain aspects which the Working Party wishes to bring to the notice of the Committee.

19.2. Foods for the young infant should be clearly identifiable as such and the user left in no doubt as to the way in which they should be used. Consideration will need to be given to the inclusion on the label of some positive indication as to suitability for feeding infants, for example, a statement such as 'suitable for feeding infants' or even of a readily recognizable symbol.

19.3. Should a manufacturer declare nutritional information on the label, such information should be expressed in a standard form, preferably /100 ml of reconstituted feed.

19.4. Full information covering both nutrients and ingredients (preferably expressed /100 ml of reconstituted feed) should in any case be available from manufacturers to those who require it (professional persons and others). Nearly all manufacturers are already co-operative in this respect and make such information readily available.



19.5. Instructions on the label should be concise, uniform and easily understood, and should include a statement that only water and no other substance is to be added when reconstituting a feed.

19.6. The volume of food required by the infant should be given as a range for different weight categories. These instructions should be so worded that the mother understands that a variation in the total volume of feed is allowable to take into account the individual needs of her infant.

19.7. The Working Party is concerned about the promotional aspects of labelling, and strongly deprecates the placing of any material on a label which might persuade a mother that manufactured milks are equivalent to or superior to human milk or which might deter a mother from breast feeding. Labels should not carry words or pictures which could suggest that infants who are given any particular infant formula are likely to be more contented, or grow larger and stronger than those who are breast-fed.



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## V Conclusions

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### 20. Summary

20.1. The report refers to foods which can be used as the sole source of nourishment for healthy young infants who for any reason are not receiving an adequate supply of breast milk.

20.2. In *Part I*, the following definitions have been agreed (para 2.2.1):

- (a) an infant is a child who has not attained the age of one year,
- (b) a young child is a child from the age of one to three years.

20.3. Terms used in the report, for example, the young infant, the older infant, the low birthweight infant, infant formula, special infant formula are explained in section 2.3 of the report.

20.4. Artificial feeding can be associated with hazards to health. The composition of foods which are intended to be the sole source of nourishment for the healthy young infant should be similar to the average composition of mature human milk. Compositional guidelines rather than an exact standard have been recommended (paras 3.1.2 to 3.1.8 and 3.3.1 to 3.3.3).

20.5. Foods for the young infant which comply with the compositional guidelines may nevertheless be unsuitable as a complete substitute for human milk. The biological value could be different from that expected when nutrient composition alone is considered. Both biological and clinical evaluation of all products is therefore necessary, and is indeed present practice. Most manufacturers make thorough trials before introducing new foods or modifications of those already in production (para 3.4.1 to 3.4.7).

20.6. The Working Party is of the opinion that all foods which are manufactured as the sole source of nourishment for the young infant should be subjected to scrutiny even though the composition accords with the guidelines (paras 3.5.1 to 3.5.5). This would involve the setting up of an expert panel which would have the task of assessing nutrient composition and the results of feeding trials, of suggesting further tests or an independent verification of tests where necessary, of ensuring the continued suitability of products and of keeping in touch with the results of further research and advances in knowledge in order to update the compositional guidelines whenever appropriate.

20.7. *Part II* of the report (sections 4 to 14) gives a detailed discussion of the facts upon which compositional guidelines for the energy content and nutrient



composition of any artificial feed are based. Table 4 sets out the guidelines compared with the composition of human milk.

20.8. Although some infants are fully satisfied by breast or bottle-feeding until about 6 months of age, the requirements of many infants from about 3 to 4 months onwards are not always fully met by milk alone and a mixed diet is introduced. In addition to solids, the young infant who is artificially fed requires infant formula until at least about six months of age. The mixed diet of an older infant may and often does include infant formula throughout infancy.

20.9. *Part III* of the report discusses foods for young infants which do not contain any nutrients from cows' milk or even from the milk of any other mammal. Ingredients such as the protein from the soya bean may be used. Compositional guidelines for these foods are likely to need some modification and special attention would need to be given, for example, to the biological value and amino acid composition of the protein (paras 15.1 to 15.5). Such foods would also be subject to scrutiny.

20.10. Some infants, as a result of abnormal physiological conditions cannot tolerate human milk and therefore have special dietary requirements. The feeding of all such infants would be under medical supervision. Foods which are suitable for these infants may in some cases be marketed and prescribed as medicines. These foods would be subjected to scrutiny by the Panel in the same way as other infant formulae (paras 16.1 to 16.6).

20.11. *Part IV* of the report deals with the reconstitution of infant feeds, and also with non-nutritional aspects of infant formulae. These aspects are considered only briefly because they are largely the responsibility of the Food Standards Committee and the Food Additives and Contaminants Committee (paras 17.1 to 17.3). Most infant formulae are sold as dry powders or as concentrated liquids. There are problems associated with the reconstitution of the feed and there is a need to minimize the possibility of errors in this respect. Instructions for filling scoops and the number of scoops used for a given volume of feed have been standardized. Scoop sizes are the same for all products except one (paras 18.1 to 18.3).

20.12. The solute content of domestic water used in reconstitution will affect the final composition of the artificial feed. This may be of importance if the sodium content of domestic water used for reconstituting feeds is such that the upper limit of the guideline for sodium would be appreciably exceeded (paras 13.1.1 to 13.1.4).

20.13. The labelling of food is mainly a matter for the Food Standards Committee but there is concern that foods for the young infant, which are their sole source of nourishment, should be clearly identifiable as such (para 19.2) and that information about reconstitution and any feeding chart should be concise and easily understood. Instructions could well be pictorial and should indicate that the volume of food may be greater or smaller for any particular infant than is shown on the chart for a particular age (paras 19.5 and 19.6).



20.14 No labelling, advertisement or promotional literature should indicate or imply that, for a healthy young infant, an infant formula is to be preferred to human milk, or that artificial feeding is to be preferred to breast feeding (para 19.7).

## 21. Recommendations

21.1. All foods which are intended for sale as the sole source of nourishment for the young infant should be subjected to scrutiny by a panel of experts.

21.2. The compositional guidelines set out in Table 4 should be used in the formulation of any food for young infants. The guidelines should **not** be regarded as a fixed standard and should be kept under review as knowledge increases. Problems about the inclusion of 'overages', that is to say amounts over and above the upper limit guidelines for any particular nutrient in order to ensure that at least the lower limit would be met after the normal shelf life, would be discussed between manufacturer and the Scrutiny Panel.

21.3. Nutritional evaluation of the product should be in terms of the ingredients used in production, the nutrient composition of the product, the results of laboratory and animal tests and the results of feeding trials. Only on the advice of the Scrutiny Panel could a product be accepted for marketing as suitable for young infants.

21.4. No substance other than water should be needed for the reconstitution of a feed. The procedure for reconstitution should be uniform.

21.5. Instructions on the label for the reconstitution of a food should be simple and easy to follow.

21.6. No label, advertisement or promotional literature should imply that a product is equivalent to or superior to the milk of a healthy mother, or carry words or pictures which might deter a mother from breast feeding, or suggest by any means that artificially fed infants are more likely to be contented, or grow faster or larger than breast-fed infants.



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## Appendix 1: Tables

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- Table 1:** The amounts of water, total nitrogen, protein, fat, carbohydrate, the energy value and the amounts of non-protein non-amino acid nitrogen and of cholesterol in 100 ml of pooled mature human and cow's milk.
- Table 1A:** as Table 1 but in SI units
- Table 2:** The amounts of some of the vitamins in pooled mature human and cows' milk (expressed as mg or  $\mu\text{g}/100$  ml).
- Table 3:** The amounts of some inorganic nutrients in mature human and cows' milk (expressed as mg or  $\mu\text{g}$  per 100 ml).
- Table 3A:** as Table 3 but in SI units
- Table 4:** The composition of mature human milk and the nutritional guidelines for infant formulae.

**Table 1:** The amounts of water, total nitrogen, protein, fat and carbohydrate, the energy value and the amounts of non-protein non-amino acid nitrogen and of cholesterol in 100 ml of pooled mature human and cows' milk.

	Water	Total <sup>1</sup> nitrogen	Non-protein non-amino acid nitrogen <sup>2</sup>	Protein <sup>3</sup>	'Actual' protein <sup>4</sup>	Fat	Carbohydrate <sup>5</sup>	Energy <sup>6</sup>	Cholesterol
	g	g	mg	g	g	g	g	kcal	mg
Human milk mean	89.7	0.21	46	1.3	1.07	4.2	7.4	70	16
range	89.3-	0.19-	41-	1.2-	0.95-	3.7-	7.1-	65-	12-
of means	90.1	0.22	55	1.4	1.20	4.8	7.8	75	23
Cows' milk mean	90.2	0.54	-	3.4	3.0	3.9	4.8	67	14
range	-	-	.40-	-	-	-	-	-	-
			50						

<sup>1</sup>Determined by Kjeldahl method.

<sup>2</sup>see para 6.1

<sup>3</sup>Total nitrogen x 6.38

<sup>4</sup>protein in human milk is calculated from total amino acid nitrogen ie free amino acids plus those derived from hydrolysis of milk protein multiplied by the factor 6.38; protein in cows' milk is calculated from total N (including non-amino acid nitrogen) multiplied by the factor 6.38.

<sup>5</sup>Expressed as monosaccharide.

<sup>6</sup>Calculated by applying the modified Atwater factors (Southgate and Durnin, 1970):

protein 4 kcal per g;

fat 9 kcal per g;

carbohydrate as monosaccharide 3.75 kcal per g.

Source: Human milk - Department of Health and Social Security (1977)

Cows' milk - derived from Paul and Southgate (1978)



**Table 1A:** The amounts of water, total nitrogen, protein, fat, carbohydrate, the energy value and the amounts of non-protein non-amino acid nitrogen and of cholesterol per litre in pooled mature human milk and in cows' milk.

	Water	Total <sup>1</sup> nitrogen	Non-protein non-amino acid nitrogen <sup>2</sup>	Protein <sup>3</sup>	'Actual' protein <sup>4</sup>	Fat	Carbohydrate <sup>5</sup>	Energy <sup>6</sup>	Cholesterol
	g	g	mg	g	g	g	g	kJ	mmol
Human milk									
mean	897	2.1	460	13	10.7	42	74	290	0.42
range									
of means	893–901	1.9–2.2	410–550	12–14	9.5–12	37–48	71–78	270–315	0.31–0.60
Cows' milk									
mean	902	5.4	—	34	30	39	48	280	0.36
range	—	—	400–500	—	—	—	—	—	—

<sup>1</sup>Determined by Kjeldahl method

<sup>2</sup>see para 6.1

<sup>3</sup>Total nitrogen x 6.38

<sup>4</sup>Protein in human milk is calculated from total amino acid nitrogen ie free amino acids plus those derived from hydrolysis of milk protein multiplied by the factor 6.38; protein in cows' milk is calculated from total N (including non-amino acid nitrogen) multiplied by the factor 6.38.

<sup>5</sup>Expressed as monosaccharide

<sup>6</sup>Calculated by applying the modified Atwater factors (Royal Society, 1972)

protein = 17 kJ per g

fat = 37 kJ per g

carbohydrate as monosaccharide = 16 kJ per g

Source: Human milk – Department of Health and Social Security (1977)

Cows' milk – derived from Paul and Southgate (1978).

**Table 2: The amounts of some of the vitamins in pooled mature human and cows' milk (expressed as mg or  $\mu\text{g}/100\text{ ml}$ )**

	Retinol $\mu\text{g}$	$\alpha$ -tocopherol mg	Vitamin C mg	Thiamin $\mu\text{g}$	Riboflavin $\mu\text{g}$	Nicotinic acid mg	Vitamin B6 $\mu\text{g}$	Vitamin B12 $\mu\text{g}$	Folic acid (total) $\mu\text{g}$	Panathothenic acid mg	Biotin $\mu\text{g}$
Human milk mean	60	0.35	3.8	16	31	0.23	5.9	0.01	5.2	0.26	0.76
range of means	40- 76	0.29- 0.39	3.1- 4.5	13- 21	-	0.21- 0.27	5.1- 7.2	-	3.1- 6.2	0.22- 0.33	0.52- 1.13
Cows' milk mean	31	0.09	2.0	40	190	0.08	40	0.3	5	0.35	2.0
range summer winter	35- 26	0.10- 0.07	-	30- 60	150- 230	0.06- 0.13	21- 72	-	-	0.2- 0.5	1.0- 3.0

Source: Human milk - Department of Health and Social Security (1977)  
Cows' milk - derived from Paul and Southgate (1978)



**Table 3: The amounts of some inorganic nutrients in pooled mature human and cows' milk (expressed as mg or  $\mu\text{g}/100\text{ ml}$ )**

	Na mg	K mg	Cl mg	Ca mg	Mg mg	P mg	Fe $\mu\text{g}$	Cu $\mu\text{g}$	Zn $\mu\text{g}$	Se $\mu\text{g}$	I $\mu\text{g}$	F $\mu\text{g}$
Human milk mean	15	60	43	35	2.8	15	76	39	295	1.4	7	7.7
range of means	11- 20	57- 62	35- 55	32- 36	2.6- 3.0	14- 15	62- 93	37- 43	260- 330	0.8- 1.9	2- 12	2.1 15.5
Cows' milk mean	50	150	95	120	12	95	50	20	350	*	26*	*
range	35- 90	110- 170	90- 110	110- 130	9- 14	90- 100	30- 60	10- 60	200- 600	0.5- 5	*	3- 22

Source: Human milk - Department of Health and Social Security (1977)

Cows' milk - derived from Paul and Southgate (1978), references for figures for selenium, iodine and fluorine are given in Table 12.1 p. 49.

\*The content varies considerably with the diet of the cow

**Table 3A:** *The amounts per litre of some inorganic nutrients in pooled mature human milk and in cows' milk*

	Na	K	Cl	Ca	Mg	P	Fe	Cu	Zn	Se	F	I
	mmol	mmol	mmol	mmol	mmol	mmol	$\mu$ mol	$\mu$ mol	$\mu$ mol	$\mu$ mol	$\mu$ mol	$\mu$ mol
Human milk mean	6.5	15.4	12.1	8.8	1.2	4.8	13.6	6.1	45.4	0.18	4.1	0.55
range	4.8–	14.6–	9.9–	8.0–	1.1–	4.5–	11.1–	5.8–	40.0–	0.10–	1.1–	0.16–
of means	8.7	15.9	15.5	9.0	1.3	4.8	16.6	6.8	50.8	0.24	8.2	0.94
Cows' milk mean	21.7	38.5	26.8	30.0	5.0	30.6	8.9	3.1	53.8	*	*	2.0*
range	15.2–	28.2–	25.4–	27.5–	3.8–	29.0–	5.4–	1.6–	30.8	0.06–	1.6–	*
	39.1	43.6	31.0	32.5	5.8	32.3	10.7	9.4	92.3	0.63	11.6	*

Source: Human milk – Department of Health and Social Security (1977)  
Cows' milk – Paul and Southgate (1978)

\*The content varies considerably with the diet of the cow



**Table 4: Nutritional guidelines for the composition of artificial feeds compared with the composition of mature human milk**

		Guidelines for artificial feed/100 ml		Composition of pooled samples of mature human milk <sup>(6)</sup>		
		minimum	maximum	mean	minimum	maximum
Water	g	NS	NS	89.7	89.3	90.1
Energy	kJ	270	315	290	270	315
	kcal	65	75	70	65	75
Protein	g	1.5	2.0 <sup>1</sup>	1.07	0.95	1.20
	g	1.2	2.0 <sup>2</sup>			
Carbohydrate <sup>3</sup> lactose total	g	2.5	8.0	7.4	7.1	7.8
	g	4.8	10.0			
Fat	g	2.3	5.0 <sup>4</sup>	4.2	3.7	4.8
Vitamins - fat soluble						
A (retinol equivalent)	µg	40	150	60	40	76
D	µg	0.7	1.3	NE	NE	NE
E (α-tocopherol)	mg	0.3 <sup>5</sup>	NS	0.35	0.29	0.39
K	µg	1.5	NS	NE	NE	NE
Vitamins -						
thiamin	µg	13	NS	16	13	21
riboflavin	µg	30	NS	31	31	31
nicotinic acid	µg	230	NS	230	210	270
B <sub>6</sub>	µg	5	NS	5.9	5.1	7.2
B <sub>12</sub>	µg	0.01	NS	0.01	0.01	0.01
total folate	µg	3	NS	5.2	3.1	6.2
pantothenic acid	µg	200	NS	260	220	330
biotin	µg	0.5	NS	0.76	0.52	1.13
C	mg	3.0	NS	3.8	3.1	4.5
Major minerals						
sodium	mg	15	35	15	11	20
potassium	mg	50	100	60	57	62
chloride	mg	40	80	43	35	55
calcium	mg	30	120 <sup>6</sup>	35	32	36
phosphorus	mg	15	60	15	14	15
magnesium	mg	2.8	12	2.8	2.6	3.0
Trace nutrients <sup>7</sup>						
iron	µg	70	700	76	62	93

<sup>1</sup> cows' milk protein in which the casein to whey ratio is unadjusted  
<sup>2</sup> casein to whey ratio is similar to that of human milk  
<sup>3</sup> lactose expressed as the mono-saccharide or as lactose monohydrate (footnote to para 5.1)  
<sup>4</sup> see para 8.16  
<sup>5</sup> the ratio of α-tocopherol (mg) to polyunsaturated fatty acids (g) should be not less than 0.4:1.02  
<sup>6</sup> the ratio of calcium (mg) to phosphorus (mg) should be not less than 1.2:1.0 and not more than 2.2:1.0  
<sup>7</sup> guidelines for trace elements other than iron are not set (see paras 12.11.1 to 12.11.5)  
<sup>8</sup> Source: Department of Health and Social Security (1977)  
 NS not set  
 NE not estimated

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## **Appendix 2: Compositional limits imposed by the recommended ranges for energy, protein, fat and carbohydrate and the expression of the recommendations in terms of an energy basis per 100 kcal.**

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1. The recommendation that the energy value of an artificial feed should be within the range of 65 to 75 kcal/100 ml of reconstituted feed imposes constraints on the composition of the feed in terms of protein, fat and carbohydrate.
2. For the purpose of this appendix the energy contribution of protein ( $N \times 6.38$ ) has been taken as 7 kcal/100 ml infant feed. This is the mean of the range 1.5 g protein (6 kcal) to 2.0 g protein (8 kcal) as recommended in para 6.21. Energy calculations are made according to the convention described earlier (paragraph 5.1 of this report).
3. The energy limits for the contributions of fat and carbohydrate/100 ml reconstituted feed then become 58 kcal at the lower end and 68 kcal at the upper end of the energy range.
4. At the minimum of the carbohydrate range (para 7.12), that is to say, 4.8 g (18 kcal), at least 4.4 g fat must be present and at the maximum carbohydrate 10 g (37.5 kcal) not more than 3.4 g fat can be present.
5. By analogy the lowest fat value, at maximum carbohydrate and minimum energy, would be 2.3 g/100 ml feed.
6. There are further constraints when composition of the feed is expressed on an energy basis. If a single energy value is used in the calculations, fat and carbohydrate cannot be varied independently. For example at 65 kcal/100 ml non-protein energy is 58 kcal/100 ml. To meet this at minimum carbohydrate (4.8 g/100 ml) at least 4.4 g fat/100 ml are necessary. The minimum fat would not be permitted as this would require the carbohydrate value to be higher than the upper limit. The compositional limits at 65 kcal/100 ml are fat 2.3 to 4.4 g/100 ml and carbohydrate 4.8 to 10.0 g/100 ml feed. At 70 kcal/100 ml the limits for fat are 2.8 to 5.0 g/100 ml and for carbohydrate are 4.8 to 10.0 g/100 ml. At 75 kcal/100 ml the limits for fat are 3.4 to 5.0 g/100 ml and for carbohydrate 6.1 to 10.0 g/100 ml feed.



7. *Expression on an Energy Basis* The recommendations given in the report have been expressed, in Tables A1 to A4 of this appendix, per 100 kcal at three energy levels, ie 65, 70 and 75 kcal per 100 ml and the tables show the ranges that result from these calculations. Table A1 gives the values for fat and carbohydrate; A2 for protein; A3 for vitamins, and A4 for inorganic constituents. Table A1 has been calculated at a fixed protein concentration of 1.75 g/100 ml (= 7 kcal) for clarity. The protein range is very small as is shown in Table A2.

**Table A1:** *Recommendations expressed on a volume and an energy basis*

Energy Value kcal/100 ml	Constituent	Permitted Range <sup>1</sup> per 100 ml	Permitted range per 100 kcal	Percentage of Energy
65	fat	2.3– 4.4	3.5– 6.8	31.8–60.9
	carbohydrate	4.8–10.0	7.4–15.4	27.7–57.7
70	fat	2.8– 5.0	4.0– 7.1	36.0–64.3
	carbohydrate	4.8–10.0	6.9–14.3	25.7–53.6
75	fat	3.4– 5.0	4.5– 6.7	40.8–60.0
	carbohydrate	6.1–10.0	8.1–13.3	30.5–50.0

<sup>1</sup>at a protein concentration of 1.75g/100 ml. The protein range allowed in the guidelines permits a very minor extension of this range.

**Table A2:** *Recommendations for protein expressed on a volume and an energy basis*

Energy Value kcal/100 ml	Recommendation per 100 ml	Recommendation per 100 kcal	Percentage of Energy
65	1.5–2.0	2.3–3.1	9.2–12.3
70	1.5–2.0	2.1–2.9	8.6–11.4
75	1.5–2.0	2.0–2.7	8.0–10.7

**Table A3:** Recommended compositional limits for vitamins expressed on a volume and energy basis.

Nutrient		Recommendation per 100 ml	Recommendation on energy basis per 100 kcal		
			at 65 kcal	at 70 kcal	at 75 kcal
Vitamin A (retinol equivalent)	μg	40–150	62–231	57–214	53–200
Vitamin D	μg	0.7–1.3	1.1–2.0	1.0–1.9	0.9–1.7
α-Tocopherol	μg	0.3	0.46	0.71	0.67
Thiamin	μg	13	20	19	17
Riboflavin	μg	30	46	43	40
Nicotinic Acid	μg	250	385	357	333
Vitamin B6	μg	5	7.7	7.1	6.7
Vitamin B12	μg	0.01	0.015	0.014	0.013
Folic acid total	μg	3	4.6	4.3	4.0
Pantothenic acid	mg	0.20	0.30	0.29	0.26
Biotin	μg	0.5	0.77	0.71	0.67
Vitamin C	mg	3.0	4.6	4.3	4.0

**Table A4:** Recommended compositional limits for inorganic constituents expressed on a volume and energy bases.

Nutrient		Recommendation per 100 ml	Recommendation on energy basis per 100 kcal		
			at 65 kcal	at 70 kcal	at 75 kcal
Sodium	mg	15–35	23–54	21–50	20–47
Potassium	mg	50–100	77–153	72–143	67–133
Chloride	mg	40–80	61–123	57–115	53–107
Calcium	mg	30–120	46–185	43–171	40–160
Phosphorus	mg	15–60	23–92	21–86	20–80
Magnesium	mg	2.8–12.0	4.3–18.5	4.0–17.1	3.7–16.0
Iron	μg	70–700	108–1080	100–1000	93–930



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## Appendix 3: Milk foods for older<sup>1</sup> infants

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1. Milk continues to play an important part in the diet even when an older infant is no longer dependent upon it as the sole source of nourishment. Once the transition to other foods has been achieved most infants gradually reduce the amount of milk they consume. When solid foods are first introduced, it is customary for mothers to continue with the feeds which they gave during early infancy. However, as the infant adapts to an increasing variety of different foods and to increasing amounts of them, human milk or infant formula is no longer essential.

2. In the United Kingdom from the age of about six months to one year many bottle-fed infants may be given household milk. Pasteurized cows' milk is a suitable food for children who eat a mixed diet, and who get enough vitamin D from sunlight or vitamin supplements. It is not suitable where there is any risk of vitamin D deficiency unless vitamin supplements are taken. For the older infant there may be an advantage in the greater protein content of unmodified cows' milk or the milk of other mammals.

3. By about six months of age the iron stores of even the breast-fed infant are likely to be depleted. Solids introduced into the diet may provide an adequate amount of iron, but any 'follow-up'<sup>2</sup> milk for the older infant could with advantage be enriched with iron. Addition of vitamins A, C and D would also be of prophylactic importance especially against vitamin D deficiency in this country.

4. Unmodified cows' milk has been criticized as a food for older infants and young children on the grounds that the fat content is such that this food may predispose to obesity, and also that cows' milk is rich in saturated fatty acids which may predispose to coronary artery disease in later life. However the development of obesity is a matter of an excess total food energy intake in relation to energy expenditure and there is no evidence that young children who drink household milk become obese or necessarily run a greater risk of obesity than those who drink milk from which some fat has been removed. There is also no evidence that a diet rich in polyunsaturated fatty acids in childhood prevents coronary heart disease in later life (paragraph 8.16).

<sup>1</sup>the term 'older infant' is explained in Section 2.3.

<sup>2</sup>The FAO/WHO Codex Alimentarius Committee on Foods for Special Dietary purposes is elaborating an international standard for "follow-up or supplementary foods" intended for use by older infants.

5. Unmodified cows' milk is a food which is satisfactory for older infants (from about 6–9 months onwards) and for young children provided that the diet also includes a mixture of solid foods and that the infant has enough vitamin D. We do not consider that a highly processed milk food, as provided for in the draft Codex standard, is necessary for older infants who are eating a mixed diet. In the United Kingdom a follow-up milk food based on pasteurized cows' milk would be adequate providing it is enriched with vitamins A, C, D and with iron in the amounts recommended in the guidelines for infant formula.

6. Milk foods which are especially marketed for the older infant must be distinguished, by careful labelling, from those for the young infant. Mothers need to be advised that these foods should be given only to those who have reached at least six months of age and that they are suitable for older infants only as part of a mixed diet. Despite the fact that some infants may need other foods from four months onwards, a 'follow-up' milk intended for the older infant should not be promoted in any way that could persuade a mother that it is suitable as the sole source of nourishment for the young infant.



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## Appendix 4: References

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- Aballi, A. J., Howard, C.E. and Triplett, R.F., 1966.  
Absorption of vitamin K from the colon in the newborn infant.  
*Journal of Pediatrics*, **8**, 305–308.
- Aitchison, J. M., Dunkley, W. L., Canolty, N. L. and Smith, M. L., 1977.  
Influence of diet on trans fatty acids in human milk.  
*American Journal of Clinical Nutrition*, **30**, 2006–2015.
- Alexiou, D., Grimanis, A. P., Grimani, M., Papaevangelou, E., Koumantakis, E. and Papadatos, C., 1977.  
Trace elements (zinc, cobalt, selenium, rubidium, bromine, gold) in human placenta and newborn liver at birth.  
*Pediatric Research*, **11**, 646–648.
- American Academy of Pediatrics, Committee on Nutrition, 1976.  
Commentary on breast feeding and infant formulas, including proposed standards for formulas.  
*Pediatrics*, **57**, 278–285.
- Anast, C. S., 1964.  
Serum magnesium levels in the newborn.  
*Pediatrics*, **33**, 969–974.
- Angelieva, R. and Syarova, D., 1968.  
A study of the mineral content of human milk.  
*Khigiena i Zdraveopazvane*, **11**, 376–385.
- Archibald, J. G., 1958.  
Trace elements in milk: a review. I and II.  
*Dairy Science Abstracts*, **20**, 712–725; 798–812.
- Armstrong, M. D. and Yates, K. N., 1963.  
Free amino acids in milk.  
*Proceedings of the Society for Experimental Biology and Medicine*, **113**, 680–683.
- Arneil, G. A. and Chin, K. C., 1979.  
Lower solute milks and reduction of hypernatraemia in Glasgow infants.  
*Lancet*, **2**, 840.
- Ashkenazi, A., Levin, S., Djaldetti, M., Fishel, E. and Benvenisti, D., 1973.  
The syndrome of neonatal copper deficiency.  
*Pediatrics*, **52**, 525–533.
- Auricchio, S., Rubino, A. and Murset, G., 1965  
Intestinal glycosidase activities in the human embryo, fetus and newborn.  
*Pediatrics*, **35**, 944–954.
- Backer Dirks, O., Jongeling-Eijndhaven, J. M. P. A., Flissebaalje, T. D. and Gedalia, I., 1974.  
Total and free ionic fluoride in human and cows' milk as determined by gas-liquid chromatography and the fluoride electrode.  
*Caries Research*, **8**, 181–186.

- Bakwin, H., 1937.  
Pathogenesis of tetany in the newborn.  
*American Journal of Diseases of Children*, **54**, 1211-1226.
- Baltimore, R. S., Vecchitto, J. S. and Pearson, H. A., 1978.  
Growth of *Escherichia coli* and concentration of iron in an infant feeding formula.  
*Pediatrics*, **62**, 1072-1074.
- Banister, A., Matin-Siddiqi, S. A. and Hatcher, G. W., 1975.  
Treatment of hypernatraemic dehydration in infancy.  
*Archives of Disease in Childhood*, **50**, 179-186.
- Bartrop, D., 1974.  
Lipid composition and absorption by low birth-weight infants.  
*Pediatric Research*, **8**, 138.
- Bartrop, D. and Oppé, T. E., 1970.  
Dietary factors in neonatal calcium homeostasis.  
*Lancet*, **2**, 1333-1335.
- Bartrop, D. and Oppé, T. E., 1973.  
Absorption of fat and calcium by low birth-weight infants from milks containing butterfat and olive oil.  
*Archives of Disease in Childhood*, **48**, 496-501.
- Bartrop, D., Mole, R. and Sutton, A., 1977.  
Absorption and endogenous faecal excretion of calcium by low birth-weight infants on feeds with varying contents of calcium and phosphate.  
*Archives of Disease in Childhood*, **52**, 41-49.
- Barrie, H., Martin, E. and Ansell, C., 1975.  
Milk for babies.  
*Lancet*, **1**, 1330-1331.
- Belton, N. R., Cockburn, F., Forfar, J. O., Giles, M. M., Kirkwood, J., Smith, J., Thistlethwaite, D., Turner, T. L. and Wilkinson, E. M., 1977.  
Clinical and biochemical assessment of a modified evaporated milk for infant feeding.  
*Archives of Disease in Childhood*, **52**, 167-175.
- Berfenstam, R., 1952.  
Studies in blood zinc. A clinical and experimental investigation into the zinc content of plasma and blood corpuscles with special reference to infancy.  
*Acta Paediatrica Scandinavica*, **41**, Supplement 87, 3-97.
- Berger, H. M., Scott, P. H., Kenward, C., Scott, P. and Wharton, B. A., 1978.  
Milk pH, acid base status, and growth in babies.  
*Archives of Disease in Childhood*, **53**, 926-930.
- Berger, H. M., Scott, P. H., Kenward, C., Scott, P. and Wharton, B. A., 1979.  
Curd and whey proteins in the nutrition of low birth-weight babies.  
*Archives of Disease in Childhood*, **54**, 98-104.
- Bezkorovainy, A., 1977.  
Human milk and colostrum proteins: a review.  
*Journal of Dairy Science*, **60**, 1023-1036.
- Binnerts, W. T., 1954.  
Goitre and the iodine content of cows' milk.  
*Nature*, **174**, 973-974.



- Boersma, E. R., 1979.  
Changes in fatty acid composition of body fat before and after birth in Tanzania – an international comparative study.  
*British Medical Journal*, **1**, 850–854.
- Bonvini, E., Brughera, F. and Cantone, A., 1967.  
Acidi grassi nel latte uonio: variazioni qualitative nei primi tre mese di allattamento.  
*Pediatria Napoli*, **75**, 482–492.
- British Paediatric Association, 1956.  
Hypercalcaemia in infants and vitamin D.  
*British Medical Journal*, **2**, 149.
- British Pharmaceutical Codex, 1973.  
London, Pharmaceutical Press.
- Broadhead, G. D., Pearson, I. B. and Wilson, G. M., 1965.  
Seasonal changes in iodine metabolism. 1. Iodine content of cows' milk.  
*British Medical Journal*, **1**, 343–345.
- Broek, A. and Wolff, L. K., 1935.  
The quantity of Cu, Mn and Zn in cows' milk.  
*Acta Brevia Neerlandicade Physiologia, Pharmacologia, Microbiologia*, **5**, 80–81.
- Brueton, M. J., Berger, H. M., Brown, G. A., Ablitt, L., Iyngkaron, N. and Wharton, B. A. (1978).  
Duodenal bile acid conjugation patterns and dietary sulphur amino acids in the newborn.  
*Gut*, **19**, 95–98.
- Bullen, C. L. and Willis, A. T., 1971.  
Resistance of the breast-fed infant to gastro-enteritis.  
*British Medical Journal*, **3**, 338–343.
- Bullen, J. J., Rogers, H. J. and Leigh, L., 1972.  
Iron-binding proteins in milk and resistance to *Escherichia coli* infection in infants.  
*British Medical Journal*, **1**, 69–75.
- Burman, D., 1972.  
Haemoglobin levels in normal infants aged 3 to 24 months, and the effect of iron.  
*Archives of Disease in Childhood*, **47**, 261–271.
- Caddell, J. L., 1974.  
Magnesium in the nutrition of the child.  
*Clinical Pediatrics (Philadelphia)*, **13**, 263–267.
- Caffey, J., 1950.  
Chronic poisoning due to excess of vitamin A.  
*Pediatrics*, **5**, 672–687.
- Cartwright, G. E. and Wintrobe, M. M., 1964.  
Copper metabolism in normal subjects.  
*American Journal of Clinical Nutrition*, **14**, 224–232.
- Cavell, P. A. and Widdowson, E. M., 1964.  
Intakes and excretions of iron, copper and zinc in the neonatal period.  
*Archives of Disease in Childhood*, **39**, 496–501.
- Chilean Iodine Educational Bureau, 1952.  
Iodine content of foods.  
London, Chilean Iodine Educational Bureau.

Cockburn, F., Brown, J. K., Belton, N. R. and Forfar, J. O., 1973.  
Neonatal convulsions associated with primary disturbance of calcium, phosphorus and magnesium.  
*Archives of Disease in Childhood*, **48**, 99-103.

Connolly, R. J., 1971.  
An increase in thyrotoxicosis in Southern Tasmania after an increase in dietary iodine.  
*Medical Journal of Australia*, **1**, 1268-1271.

Coursin, D. B., 1954.  
Convulsive seizures in infants with pyridoxine-deficient diet.  
*Journal of the American Medical Association*, **154**, 406-408.

Coussons, H., 1969.  
Magnesium metabolism in infants and children.  
*Postgraduate Medicine*, **46**, 135-139.

Crawford, M. A., 1977.  
Polyunsaturated fatty acids in the brain.  
*Lancet*, **1**, 953.

Crawford, M. A., Sinclair, A. J., Msuya, P. M. and Munhambo, A., 1973.  
In: *Dietary Lipids and Postnatal Development*. Edited by C. Galli, J. Jacini and A. Pocale, p.41.  
New York, Raven.

Crawford, M. A., Hall, B., Laurence, B. M. and Munhambo, A., 1976.  
Milk lipids and their variability.  
*Current Medical Research and Opinion*, **4**, 33-43.

Dahl, L. K., 1972.  
Salt and Hypertension.  
*American Journal of Clinical Nutrition*, **25**, 231-244.

Dallman, P. R., 1974.  
Iron, vitamin E and folate in the preterm infant.  
*Journal of Pediatrics*, **85**, 742-752.

Dam, H., Dyggve, H., Larsen, H. and Plum, P., 1952.  
The relation of vitamin K deficiency to haemorrhagic disease of the newborn.  
*Advances in Pediatrics*, **5**, 129-153.

Darmady, J. M., Fosbrooke, A. S. and Lloyd, J. K., 1972.  
Prospective study of serum cholesterol levels during the first year of life.  
*British Medical Journal*, **2**, 685-688.

Davies, D. P. and Saunders, P., 1973.  
Blood urea. Normal values in early infancy related to feeding practices.  
*Archives of Disease in Childhood*, **48**, 563-565.

de Swiet, M., Fayers, P. and Cooper, L., 1977.  
Effect of feeding habit on weight in infancy.  
*Lancet*, **1**, 892-894.

Department of Health and Social Security, 1974.  
Present day practice in infant feeding.  
*Report on Health and Social Subjects, No. 9*.  
London, HMSO.



Department of Health and Social Security, 1977.  
The composition of mature human milk.  
*Report on Health and Social Subjects, No. 12.*  
London, HMSO.

Department of Health and Social Security, 1979.  
Recommended daily amounts of food energy and nutrients for groups of people in the United Kingdom.  
*Report on Health and Social Subjects, No. 15.*  
London, HMSO.

Diplock, A. T., 1974.  
The nutritional and metabolic roles of selenium and vitamin E.  
*Proceedings of the Nutrition Society, 33*, 315-322.

Dobbing, J. and Sands, J., 1973.  
The quantitative growth and development of the human brain.  
*Archives of Disease in Childhood, 48*, 757-767.

Dodd, F. H., Kingwill, R. G., Shearn, M. F. H., Morant, S. V. and Lewis, G., 1975.  
Iodine levels in milk following iodophor teat disinfection.  
*National Institute for Research in Dairying, Report 1973-74 p. 57.*

Donnell, G. N., Collado, M. and Koch, R., 1961.  
Growth and development of children with galactosemia.  
*Journal of Pediatrics, 58*, 836-844.

Downham, M. A. P. S., Scott, R., Sims, D. D., Webb, J. K. G. and Gardner, P. S., 1976.  
Breast feeding protects against respiratory syncytial virus infections.  
*British Medical Journal, 2*, 274-276.

Eckhert, C. D., Sloan, M. V., Duncan, J. R. and Hurley, L. S., 1977.  
Zinc-binding: a difference between human and bovine milk.  
*Science, 195*, 789-790.

Ehrlich, H. P., Tarver, H. and Hunt, T. K., 1972.  
Inhibitory effects of vitamin E on collagen synthesis and wound repair.  
*Annals of Surgery, 75*, 235-240.

Ericsson, Y. and Ribelius, U., 1970.  
Increased fluoride ingestion by bottle-fed infants and its effects.  
*Acta Paediatrica Scandinavica, 59*, 424-426.

European Society of Paediatric Gastro-enterology and Nutrition, ESPGAN Committee on Nutrition, 1977.  
Guidelines on infant nutrition. I. Recommendations for the composition of an adapted formula.  
*Acta Paediatrica Scandinavica. Supplement 262.*  
Stockholm, Almquist and Irskell.

Evans, G. W. and Johnson, P. E., 1976.  
Zinc-binding factor in acrodermatitis enteropathica.  
*Lancet, 2*, 1310.

Farquhar, J. W. and Ahrens, E. J. Jr., 1963.  
Effects of dietary fats on human erythrocyte fatty acid patterns.  
*Journal of Clinical Investigation, 42*, 675-685.

- Federation of United Kingdom Milk Marketing Boards, 1978.  
*United Kingdom Dairy Facts and Figures*.  
Thames Ditton, Milk Marketing Boards.
- Filer, L. J., Mattson, F. H. and Fomon, S. J., 1969.  
Triglyceride configuration and fat absorption by the human infant.  
*Journal of Nutrition*, **99**, 293-298.
- Fomon, S. J., 1974.  
*Infant Nutrition*, 2nd. edition.  
Philadelphia, W. B. Saunders.
- Fomon, S. J., Owen, G. M., Jensen, R. L. and Thomas, L. N., 1963.  
Calcium and phosphorus balance studies with normal full term infants fed pooled human milk or various formulas.  
*American Journal of Clinical Nutrition*, **12**, 346-357.
- Fomon, S. J., Thomas, L. N., Filer, L. J. Jr., Ziegler, E. E. and Leonard, M. T., 1971.  
Food consumption and growth of normal infants fed milk-based formulas.  
*Acta Paediatrica Scandinavica. Supplement*, **223**, 1-36.
- Food and Agriculture Organization, World Health Organization, 1972.  
Evaluation of Food Additives.  
*WHO Technical Report Series No. 488*.  
Geneva, FAO/WHO.
- Food and Agriculture Organization, World Health Organization, 1973.  
Energy and protein requirements.  
*World Health Organisation Technical Report Series, No. 522*.  
Geneva, FAO/WHO.
- Food and Agriculture Organization, World Health Organization, 1976.  
Recommended international standards for foods for infants and children.  
*Joint FAO/WHO Food Standards Programme. Codex Alimentarius Commission*.  
Rome, FAO.
- Food and Drugs Act 1955.  
London, H.M.S.O.
- Forbes, R. M., Cooper, A. R. and Mitchell, H. H., 1954.  
On the occurrence of beryllium, boron, cobalt and mercury in human tissues.  
*Journal of Biological Chemistry*, **209**, 857-865.
- Forbes, R. M., Mitchell, H. H. and Cooper, A. R., 1956.  
Further studies on the gross composition and mineral elements of the adult human body.  
*Journal of Biological Chemistry*, **223**, 969-975.
- Fosbrooke, A. S. and Wharton, B. A., 1975.  
'Added lactose' and 'added sucrose' cows' milk formulae in nutrition of low birth-weight babies.  
*Archives of Disease in Childhood*, **50**, 409-418.
- Freis, E. D., 1976.  
Salt volume and the prevention of hypertension.  
*Circulation*, **53**, 589-595.
- Fuerth, J. H., 1972.  
Iron supplementation of the diet in full-term infants: a controlled study.  
*Journal of Pediatrics*, **80**, 974-979.



- Gamble, C. T., Hansard, S. L., Moss, B. R., Davis, D. J. and Lidvall, E. R., 1971.  
Manganese utilisation and placental transfer in the gravid gilt.  
*Journal of Animal Science*, **32**, 84-87.
- Gaull, G. E., Sturman, J. A. and R  ih  , N. C. R., 1972.  
Development of mammalian sulfur metabolism: absence of cystathionase in human fetal tissues.  
*Pediatric Research*, **6**, 538-547.
- Gaull, G. E., Rassin, D. K., R  ih  , N. C. R. and Heinonen, K., 1977.  
Milk protein quantity and quality in low-birth-weight infants. 3. Effects of sulfur amino acids in plasma and urine.  
*Journal of Pediatrics*, **90**, 348-355.
- Gittleman, I. F. and Pincus, J. B., 1951.  
Influence of diet on the occurrence of hyperphosphatemia and hypocalcemia in the newborn infant.  
*Pediatrics*, **8**, 778-787.
- Glueck, C. J., Tsang, R., Balistreri, W. and Fallat, R., 1972.  
Plasma and dietary cholesterol in infancy: effects of low or moderate dietary cholesterol intake on subsequent response to increased dietary cholesterol.  
*Metabolism*, **21**, 1181-1192.
- Goldman, H. I. and Deposito, F., 1966.  
Hypoprothrombinemic bleeding in young infants.  
*American Journal of Diseases of Children*, **111**, 430-432.
- Goldman, H. I., Goldman, J. S., Kaufman, I. and Liebman, O. B., 1973.  
Late effects of early dietary protein intake in low birth-weight infants.  
*Pediatric Research*, **42**, 401-408.
- Goldman, A. S. and Smith, C. W., 1973.  
Host resistance factors in human milk.  
*Journal of Pediatrics*, **82**, 1082-1090.
- Grant, A. B. and Wilson, G. F., 1968.  
Selenium content of milk from cows given sodium selenate.  
*New Zealand Journal of Agricultural Research*, **11**, 733-736.
- Greenberg, S. M., Clabert, C. E., Savage, E. E. and Deuel, H. J. Jnr., 1950.  
Effect of fat level of diet on general nutrition; interrelation of linoleate and linolenate in supplying essential fatty acid requirement in rat.  
*Journal of Nutrition*, **41**, 473-486.
- Gross, S., 1968.  
The relationship between milk protein and iron content on haematologic values in infancy.  
*Journal of Pediatrics*, **73**, 521-530.
- Gunther, M. and Stanier, J. E., 1949.  
Diurnal variation in the fat content of breast milk.  
*Lancet*, **2**, 235-237.
- G  rson, C. T. and Saner, G., 1973.  
Effects of chromium supplementation on growth in marasmic protein calorie malnutrition.  
*American Journal of Clinical Nutrition*, **26**, 988-991.
- Guthrie, H. A., Picciano, M. F. and Sheehe, D., 1977.  
Fatty acid patterns of human milk.  
*Journal of Pediatrics*, **90**, 39-41.

- Hadjimarkos, D. M., 1963.  
Selenium content of human milk: possible effects on dental caries.  
*Journal of Pediatrics*, **63**, 273-275.
- Hadjimarkos, D. M., 1969.  
Selenium: a caries-enhancing trace element.  
*Caries Research*, **3**, 14-22.
- Hadjimarkos, D. M. and Bonhorst, C. W., 1961.  
The selenium content of eggs, milk and water in relation to dental caries in children.  
*Journal of Pediatrics*, **59**, 256-259.
- Hadjimarkos, D. M. and Shearer, T. R., 1973.  
Selenium in mature human milk.  
*American Journal of Clinical Nutrition*, **26**, 583-585.
- Hambidge, K. M., 1971.  
Chromium nutrition in the mother and the growing child.  
In: *Newer trace elements in nutrition*. Edited by W. Mertz and W. E. Cornatzer, p. 166.  
New York, Marcel Dekker.
- Hambidge, K. M., 1976.  
The importance of trace elements in infant nutrition.  
*Current Medical Research and Opinion*, **4**, Supplement. 1, 44-53.
- Hambidge, K. M., Hambidge, C., Jacobs, M. and Baum, J. D., 1972.  
Low levels of zinc in hair, anorexia, poor growth, and hypogeusia in children.  
*Pediatric Research*, **6**, 868-874.
- Hambidge, K. M., Walravens, P. A., Casey, C. E., Brown, R. M. and Bender, C., 1979.  
Plasma zinc concentrations of breast-fed infants.  
*Journal of Pediatrics*, **94**, 607-608.
- Hanna, F. M., Navarrete, D. A. and Hsu, F. A., 1970.  
Calcium-fatty acid absorption in full term infants fed milk and prepared formulas simulating human milk.  
*Pediatrics*, **45**, 216-224.
- Hansen, A. E., Haggard, M. E., Boelsche, A. N., Adam, D. J. D. and Wiese, H. F., 1958.  
Essential fatty acids in infant nutrition. III. Clinical manifestations of linoleic acid deficiency.  
*Journal of Nutrition*, **66**, 565-576.
- Hanson, L. A., 1976.  
*Escherichia coli* infections in childhood.  
*Archives of Disease in Childhood*, **51**, 737-743.
- Hanson, L. A., Carlsson, B., Ahlstedt, S., Svanborg, G. and Kaisser, B., 1975.  
Immune defence factors in human milk.  
In: *Modern Problems in Pediatrics*, **15**. Milk and Lactation: Symposium, Campione, September 1973. Edited by: N. Kretchmer, p. 63.  
New York, Karger.
- Harris, R. S. and Bunker, J. W., 1939.  
Vitamin D potency of human breast milk.  
*American Journal of Public Health*, **29**, 744-747.
- Henkin, R. I., Schulman, J. D., Schulman, C. B. and Bronzert, D. A., 1973.  
Changes in total, non-diffusible, and diffusible plasma zinc and copper during infancy.  
*Journal of Pediatrics*, **82**, 831-837.



- Hillman, L. and Haddad, J., 1976.  
Perinatal vitamin D metabolism III. Factors influencing late gestational human serum 25-hydroxy vitamin D.  
*American Journal of Obstetrics and Gynecology*, **125**, 196-200.
- Hodge, H. C., Smith, F. A. and Gedalia, I., 1970.  
Excretion of fluorides:  
In: World Health Organization. Fluorides and Human Health.  
*WHO Monographs Series No. 59*, p. 141.  
Geneva, World Health Organization.
- Holman, R. T., 1970.  
Biological activities of and requirements for polyunsaturated acids.  
In: *Progress in the Chemistry of Fats and Other Lipids*. Edited by R. T. Holman, Vol. 10.  
Oxford, Pergamon Press.
- Holt, L. E., Tidwell, H. C., Kirk, C. M., Cross, D. M. and Neale, S., 1935.  
Studies in fat metabolism. 1. Fat absorption in normal infants.  
*Journal of Pediatrics*, **6**, 427-480.
- Hurley, L. S., Lönnerdal, B. and Stanislawski, A. G., 1979.  
Zinc citrate, human milk and acrodermatitis enteropathica.  
*Lancet*, **1**, 677-678.
- Hytten, F. E., 1954.  
Clinical and chemical studies in human lactation. II. Variation in major constituents during a feeding.  
*British Medical Journal*, **1**, 176-179.
- Insull, W. Jr., Hirsch, J., James, T. and Ahrens, E. H., Jr., 1959.  
The fatty acids of human milk. II. Alterations produced by manipulation of calorie balance and exchange of dietary fats.  
*Journal of Clinical Investigation* **38**, 443-450.
- Ironside, A. G., Tuxford, A. F. and Heyworth, B., 1970.  
A survey of infantile gastroenteritis.  
*British Medical Journal*, **3**, 20-24.
- Iwarsson, K. and Ekman, L., 1974.  
Iodophor teat dipping and the iodine concentration in milk.  
*Nordisk Veterinaer Medicin*, **26**, 31-38.
- Johnson, P. E. and Evans, G. W., 1978.  
Relative zinc availability in human breast milk, infant formulas and cows' milk.  
*American Journal of Clinical Nutrition*, **31**, 416-421.
- Jennes, R., 1974.  
The composition of milk.  
In: *Lactation, a comprehensive treatise*. Edited by B. L. Larson and V. R. Smith, Vol. 3, p. 3.  
London and New York, Academic Press.
- Karpel, J. T. and Peden, V. H., 1972.  
Copper deficiency in long-term parenteral nutrition.  
*Journal of Pediatrics*, **80**, 32-36.
- Keenan, W. J., Jewett, T. and Glueck, H. I., 1971.  
Role of feeding and vitamin K in hypoprothrombinemia of the newborn.  
*American Journal of Diseases of Children*, **121**, 271-277.

- Khurshid, M., Lee, T. J., Peake, I. R. and Bloom, A. L., 1975.  
Vitamin E deficiency and platelet functional defect in a jaundiced infant.  
*British Medical Journal*, **4**, 19-21.
- Klevay, L. M., 1973.  
Hypercholesterolemia in rats produced by an increase in the ratio in zinc to copper ingested.  
*American Journal of Clinical Nutrition*, **26**, 1060-1068.
- Knopf, K., Sturman, J. A., Armstrong, M. and Hayes, K. C., 1978.  
Taurine: an essential nutrient for the cat.  
*Journal of Nutrition*, **108**, 773-778.
- Kon, S. K. and Mawson, E. H., 1950.  
Human milk.  
*Special Report Series of the Medical Research Council*, No. 269.  
London, HMSO.
- Kon, S. K., 1972.  
Milk and milk products in human nutrition.  
*FAO nutritional studies*, No. 27.  
Rome, FAO.
- Kramer, B., Sobel, A. E. and Gottfried, S. P., 1947.  
Serum levels of vitamin A in children: a comparison following oral and intramuscular administration of vitamin A in oily and aqueous mediums.  
*American Journal of Diseases of Children*, **73**, 543-553.
- Kramer, M., Szoke, K., Lindner, K. and Tarjan, R., 1965.  
The effect of different factors on the composition of human milk and its variations. 3. Effect of dietary fats on the lipid composition of human milk.  
*Nutritio et Dieta*, **7**, 71-79.
- Kummerow, F. A., 1974.  
Current studies on relation of fat to health.  
*Journal of the American Oil Chemists Society*, **51**, 255-259.
- Lakdawala, D. R. and Widdowson, E. M., 1977.  
Vitamin D in human milk.  
*Lancet*, **1**, 167-168.
- Lake, A. M., Stuart, M. J. and Oski, F. A., 1977.  
Vitamin E deficiency and enhanced platelet function: Reversal following E supplementation.  
*Journal of Pediatrics*, **90**, 722-725.
- Lamprey, M. S. and Walker, B. L., 1976.  
A possible essential role for dietary linolenic acid in the development of the young rat.  
*Journal of Nutrition*, **106**, 86-93.
- Lealman, G. T., Logan, R. W., Hutchison, J. H., Kerr, M. M., Fulton, A. M. and Brown, C. A., 1976.  
Calcium, phosphorus, and magnesium concentrations in plasma during first week of life and their relation to type of milk feed.  
*Archives of Disease in Childhood*, **51**, 377-384.
- Le Boulch, N., Gulat-Marnay, C. and Raoul, Y., 1974.  
Dérivés de la vitamine D<sup>3</sup> des laits de femme et de vache: ester sulfate de cholecalciferol et hydroxy-25-cholecalciferol.  
*International Journal for Vitamin and Nutrition Research*, **44**, 167-179.



- Lengemann, F. W., Wasserman, R. H. and Comar, C. L., 1959.  
Studies on the enhancement of radiocalcium and radiostrontium absorption by lactose in the rat.  
*Journal of Nutrition*, **68**, 443-456.
- Lewis, J. S., 1969.  
An E/PUFA ratio of 0.4 maintains normal plasma tocopherol levels in growing children.  
*Federation Proceedings*, **28**, 758.
- Lightwood, R. C., 1952.  
Idiopathic hypercalcaemia in infants with failure to thrive.  
*Archives of Disease in Childhood*, **27**, 302-303.
- Ling, E. R., Kon, S. K. and Porter, J. W. G., 1961.  
In: *Milk. The mammary gland and its secretion*. Edited by S. K. Kon and A. T. Cowie, Vol. II, p. 204.  
New York and London, Academic Press.
- Lipsitz, P. J., 1971.  
The clinical and biochemical effects of excess magnesium in the newborn.  
*Pediatrics*, **47**, 501-509.
- Lloyd, J. K., 1976.  
Hyperlipoproteinaemia and atherosclerosis.  
In: *Recent Advances in Paediatrics*, No. 5. Edited by D. Hull, p. 339.  
London, Churchill Livingstone.
- Lo, S. S., Frank, D. and Hitzig, W. H., 1973.  
Vitamin E and haemolytic anaemia in premature infants.  
*Archives of Disease in Childhood*, **48**, 360-365.
- Lombeck, I., Kasperek, K., Harbisch, H. D., Feinendegen, L. E. and Bremer, H. J. 1977.  
The selenium state of healthy children. I. Serum selenium concentration at different ages; activity of glutathione peroxidase of erythrocytes at different ages; selenium content of food of infants.  
*European Journal of Pediatrics*, **125**, 81-88.
- Lönnerdal, B., Forsum, E. and Hambraeus, L., 1976.  
The protein content of human milk. I. A transversal study of Swedish normal material.  
*Nutrition Reports International*, **13**, (2) 125-134.
- Macaulay, D. and Blackhall, M., 1961.  
Hypernatraemic dehydration in infantile gastro-enteritis.  
*Archives of Disease in Childhood*, **36**, 543-550.
- Macaulay, D. and Watson, M., 1967.  
Hypernatraemia in infants as a cause of brain damage.  
*Archives of Disease in Childhood*, **42**, 485-491.
- Mackenzie, H. A., 1970.  
*Milk Proteins — Chemistry and Molecular Biology*.  
New York and London, Academic Press.
- Macy, I. G., 1949.  
Composition of human colostrum and milk.  
*American Journal of Diseases of Children*, **78**, 589 - 603.
- Macy, I. G. and Kelly, H. J., 1961.  
Human and cows' milk in infant nutrition. In: *Milk the mammary gland and its secretion*.  
Edited by S. K. Kon and A. T. Cowie, Volume II p. 265.  
New York, Academic Press.

- Macy, I. G., Kelly, H. J. and Sloan, R. E., 1953.  
The Composition of milks.  
*National Research Council Publication, No. 254.*  
Washington, D.C., National Academy of Sciences.
- Matthew, D. J., Taylor, B., Norman, A. P., Turner, M. W. and Soothill, J. F., 1977.  
Prevention of eczema.  
*Lancet*, **1**, 321-324.
- Mawer, E. B., Backhouse, J., Holman, C. A., Lumb, G. A. and Stanbury, S. W., 1972.  
The distribution and storage of vitamin D and its metabolites in human tissues.  
*Clinical Science*, **43**, 413-431.
- McCance, R. A. and Widdowson, E. M., 1957.  
Hypertonic expansion of the extracellular fluids.  
*Acta Paediatrica Scandinavica*, **46**, 337-353.
- McCance, R. A. and Widdowson, E. M., 1967.  
The composition of foods.  
*Special Report Series of the Medical Research Council, No. 297.*  
London, HMSO.
- McClelland, D. B. L., McGrath, J. and Samson, R. R., 1978.  
Antimicrobial factors in human milk.  
*Acta Paediatrica Scandinavica, Supplement 271*, pp. 1-20.
- McClure, F. J., 1970.  
National Institute of Dental Research, Department of Health, Education and Welfare.  
*Water fluoridation: The search and the victory.*  
Washington D.C. 1979, U.S. Government Printing Office.
- McLeod, B. E. and Robinson, M. F., 1972.  
Dietary intake of manganese by New Zealand infants during the first six months of life.  
*British Journal of Nutrition*, **27**, 229-232.
- McMillan, J. A., Landaw, S. A. and Oski, F. A., 1976.  
Iron sufficiency in breast-fed infants and the availability of iron from human milk.  
*Pediatrics*, **58**, 686-691.
- McWhirter, W. R., 1975.  
Plasma tocopherol in infants and children.  
*Acta Paediatrica Scandinavica*, **64**, 446-448.
- Mellander, O., Vahlquist, B. O. and Mellbin, T., 1959.  
Breast feeding and artificial feeding. The Norbotten Study.  
*Acta Paediatrica Scandinavica*, **48**, Supplement 116, 1-108.
- Menkes, J. M., Welcher, D. W., Levi, H. S., Dallas, J. and Gretskey, N. E., 1972.  
Relationship of elevated blood tyrosine to the ultimate intellectual performance of premature infants.  
*Pediatrics*, **49**, 218-224.
- Merrill, A. L. and Watt, B. K., 1955.  
Energy value of foods - basis and derivation.  
*US Department of Agriculture, Agriculture Handbook No. 74.*  
Washington, D.C.



- Mertz, W., 1974a.  
Biological function of nicotinic acid (NA) – chromium complexes.  
*Federation Proceedings*, **33**, 659.
- Mertz, W., 1974b.  
The newer trace elements, chromium, tin, vanadium, nickel and silicon.  
*Proceedings of the Nutrition Society*, **33**, 307–313.
- Mettler, A. E., 1976.  
Infant milk powder feeds compared on a common basis.  
*Postgraduate Medical Journal*, **52**, Supplement 8.
- Millar, K. R. and Sheppard, A. D., 1972.  
 $\alpha$ -tocopherol and selenium levels in human and cows' milk.  
*New Zealand Journal of Science*, **15**, 3–15.
- Miller, V. and Holzel, A., 1974.  
Growth and development of endodermal structures. In: *Scientific Foundations of Paediatrics*.  
Edited by J. A. Davis and J. Dobbing, p. 281.  
London, William Heinemann Medical Books Ltd.
- Mills, C. F. and Williams, R. B., 1971.  
Problems in the determination of the trace element requirements of animals.  
*Proceedings of the Nutrition Society*, **30**, 83–91.
- Ministry of Health and Department of Health for Scotland, 1957.  
*Report of the Joint Sub-Committee on Welfare Foods*.  
London, HMSO.
- Morris, E. R. and O'Dell, B. L., 1963.  
Relationship of excess calcium and phosphorus requirements to magnesium requirement and toxicity in guinea-pigs.  
*Journal of Nutrition*, **81**, 175–181.
- Morris-Jones, P. H., Houston, I. B. and Evans, R. C., 1967.  
Prognosis of the neurological complications of acute hypernatraemia.  
*Lancet*, **2**, 1385–1389.
- Morrison, S. D., 1952.  
Human Milk.  
*Commonwealth Bureau of Animal Nutrition. Technical Communication No. 18*.  
Aberdeen, University Press.
- Moxon, A. L. and Olson, V. E., 1974.  
Selenium in Agriculture. In: *Selenium*. Edited by R. A. Zingaro and W. C. Cooper, p. 675.  
New York, van Nostrand.
- Moynahan, E. J., 1974.  
Acrodermatitis enteropathica: a lethal inherited human zinc-deficiency disorder.  
*Lancet*, **2**, 399–400.
- Naismith, D. J., 1973.  
Kwashiorkor in western Nigeria: a study of traditional weaning foods with particular reference to energy and linoleic acid.  
*British Journal of Nutrition*, **30**, 567–576.

- Naismith, D. J., Deeprose, S. P., Supramaniam, G. and Williams, M. J. H., 1978.  
Reappraisal of the linoleic acid requirements of the young infant with particular regard to the use of modified cows' milk formulae.  
*Archives of Disease in Childhood*, **53**, 845-849.
- National Academy of Sciences, 1974.  
*Recommended Dietary Allowances*.  
Washington, D.C., National Academy of Sciences.
- Ogra, S. S., Weintraub, D. and Ogra, P. L., 1977.  
Immunologic aspects of human colostrum and milk. III. Fats and absorption of cellular and soluble components in the gastrointestinal tract of the newborn.  
*Journal of Immunology*, **119**, 245-248.
- Oliver, I., Sperling, O., Liberman, U.A., Frank, M. and de Bres, A., 1971.  
Deficiency of xanthine oxidase activity in colostrum of a xanthinuric female.  
*Biochemical Medicine*, **5**, 279-280.
- Oppé, T. E. and Redstone, D., 1968.  
Calcium and phosphorus levels in healthy newborn infants given various types of milks.  
*Lancet*, **1**, 1045-1048.
- Oski, F. A. and Barness, L. A., 1967.  
Vitamin E deficiency: a previously unrecognised cause of hemolytic anemia in the premature infant.  
*Journal of Pediatrics*, **70**, 211-220.
- Parkash, S. and Jenness, R., 1967.  
Status of zinc in cows' milk.  
*Journal of Dairy Science*, **50**, 127-134.
- Patrick, G. and Stirling, C., 1973.  
The dependence of calcium influx into rat intestine on sugars and alkali metals.  
*Archives Internationales de Physiologie et de Biochimie (Liège)*, **81**, 453-467.
- Paul, A. A. and Southgate, D.A.T., 1978.  
*The Composition of Foods*.  
London, HMSO.
- Paulsrud, J. R., Pensler, L., Whitten, C. F., Stewart, S. and Holman, R. T., 1972.  
Essential fatty acid deficiency in infants produced by fat-free intravenous feeding.  
*American Journal of Clinical Nutrition*, **25**, 897-904.
- Pavey, D. E., 1979.  
*Influence of dietary fat on fatty acid composition of body lipids in early life*.  
Ph.D. Thesis, Cambridge University.
- Pavey, D. E., Widdowson, E. M. and Robinson, M. P., 1976.  
Body lipids of guinea pigs exposed to different dietary fats from mid-gestation to 3 months of age.  
II. The fatty acid composition of the lipids of liver, plasma, adipose tissue and red cell membranes at birth.  
*Nutrition and Metabolism*, **20**, 351-363.
- Pearson, H. A., 1971.  
Iron-fortified formulas in infancy.  
*Journal of Pediatrics*, **79**, 557-559.



- Persson, B., Tunnel, R. and Ekegren, K., 1965.  
Chronic vitamin A intoxication during the first half year of life: description of 5 cases.  
*Acta Paediatrica Scandinavica*, **54**, 49-60.
- Petrich, C., von Voss, H., Lietke, K. and Göbel, U., 1976.  
Vitamin E concentrations in term and preterm newborns and their clinical course.  
*European Journal of Pediatrics*, **122**, 275-279.
- Pikaar, N. A. and Fernandes, J., 1966.  
Influence of different types of dietary fat on the fatty acid composition of some serum lipid fractions in infants and children.  
*American Journal of Clinical Nutrition*, **19**, 194-204.
- Potter, J. M. and Nestel, P. J., 1976.  
The effects of dietary fatty acids and cholesterol on the milk lipids of lactating women and the plasma cholesterol of breast-fed infants.  
*American Journal of Clinical Nutrition*, **29**, 54-60.
- Prasad, A. S., Halsted, J. A. and Nadimi, M., 1961.  
Syndrome of iron deficiency anemia, hepatosplenomegaly, hypogonadism, dwarfism and geophagia.  
*American Journal of Medicine*, **31**, 532-546.
- Pratt, E. L. and Snyderman, S. E., 1953.  
Renal water requirements of infants fed evaporated milk with and without added carbohydrate.  
*Pediatrics*, **11**, 65-69.
- Pullan, C. R., Dellagrammatikas, H. and Steiner, H., 1977.  
Survey of gastro-enteritis in children admitted to hospital in Newcastle-upon-Tyne 1971-75.  
*British Medical Journal*, **1**, 619-621.
- Purvis, R. J., Barrie, W. J. McK., Mackay, G. S., Wilkinson, E. M., Cockburn, F., Belton, N. R. and Forfar, J. O., 1973.  
Enamel hypoplasia of the teeth associated with neonatal tetany: a manifestation of maternal vitamin D deficiency.  
*Lancet*, **2**, 811-814.
- Räihä, N. C. R., 1971.  
The development of some enzymes of aminoacid metabolism in the human liver.  
In: *Metabolic processes in the foetus and newborn infant*. 3rd Nutricia Symposium.  
Edited by J. H. P. Jonxis, H. K. A. Visser and J. A. Troelstra, p. 26.  
Leiden, Stenfart Kroese.
- Räihä, N. C. R., Heinonen, K., Rassin, D. K. and Gaull, G. E., 1976.  
Milk protein quality and quantity in low birth-weight infants. I. Metabolic responses and effects on growth.  
*Pediatrics*, **57**, 659-674.
- Read, W. W. C., Lutz, P. G. and Tashjian, A., 1965.  
Human milk lipids. II. The influence of dietary carbohydrates and fat on the fatty acids of mature milk. A study in four ethnic groups.  
*American Journal of Clinical Nutrition*, **17**, 180-183.
- Reid, B. L., Kurnick, A. A., Suacha, R. L. and Couch, J. R., 1956.  
The effect of molybdenum on chick and poult growth.  
*Proceedings of the Society for Experimental Biology and Medicine*, **93**, 245-248.

- Reiter, B. and Oram, J. D., 1967.  
Bacterial inhibitors in milk and other biological fluids.  
*Nature*, **216**, 328-330.
- Rena, T. and Staveland, K., 1974.  
An investigation of the iodine content of milk from various places in Norway between July 1971 and June 1972.  
*Tidsskrift for den Norske Laegeforening*, **94**, 990-993.
- Rey, J. and Ricour, C., 1972.  
La spécificité moléculaire de l'absorption des graisses.  
*Biologie Gastroenterologique*, **5**, 187-204.
- Rios, E., Lipschitz, D. A., Cook, J. D. and Smith, N. J., 1975.  
Relationship of maternal and infant iron stores as assessed by determination of plasma ferritin.  
*Pediatrics*, **55**, 694-699.
- Ritchie, J. H., Fish, M. B., McMasters, V. and Grossman, M., 1968.  
Edema and hemolytic anemia in premature infants. A vitamin E deficiency syndrome.  
*New England Journal of Medicine*, **279**, 1185-1190.
- Robinson, J. E., Harvey, B. A. M. and Soothill, J. F., 1978.  
Phagocytosis and killing of bacteria and yeast by human milk cells after opsonisation in aqueous phase of milk.  
*British Medical Journal*, **1**, 1443-1445.
- Rodrigues, M. S. and Irwin, M. I., 1972.  
A conspectus of research on vitamin A requirements of man.  
*Journal of Nutrition*, **102**, 909-968.
- Rosen, J., Roginsky, M., Nathenson, G. and Finberg, L., 1974.  
25-Hydroxyvitamin D: Plasma levels in mothers and their premature infants with neonatal hypocalcaemia.  
*American Journal of Diseases of Children*, **127**, 220-223.
- Royal College of Physicians of London, 1976.  
*Fluoride, Teeth and Health*.  
London, Pitman Medical.
- Saarinen, U. M. and Siimes, M. A., 1977.  
Iron absorption from infant milk formula and the optimal level of iron supplementation.  
*Acta Paediatrica Scandinavica*, **66**, 719-722.
- Saarinen, U. M., Siimes, M. A. and Dallman, P. R., 1977.  
Iron absorption in infants: High bioavailability of breast milk iron as indicated by the extrinsic tag method of iron absorption and by the concentration of serum ferritin.  
*Journal of Pediatrics*, **91**, 36-39.
- Saarinen, U. M., Bajasaari, M., Backman, A. and Siimes, M. A., 1979.  
Prolonged breast feeding as prophylaxis for atopic disease.  
*Lancet*, **2**, 163-166.
- Sahashi, Y., Suzuki, T., Higaki, M. and Asano, T., 1967.  
Metabolism of vitamin D in animals. 5. Isolation of vitamin D sulphate from human milk.  
*Journal of Vitaminology, Japan*, **13**, 33-36.
- Sahashi, Y., Suzuki, T., Higaki, M. and Asano, T., 1969.  
Antirachitic potency of vitamin D sulfate in human milk.  
*Journal of Vitaminology, Japan*, **15**, 78-82.



- Salter, W. T., 1950.  
The chemistry and physiology of the thyroid hormone.  
In: *The hormones: physiology, chemistry and applications*. Edited by G. Pincus and K. V. Thimann, Vol. 2, p. 181.  
New York, Academic Press.
- Schlesinger, J. J. and Corelli, H. D., 1977.  
Evidence for transmission of lymphocyte responses to tuberculin by breast-feeding.  
*Lancet*, **2**, 529-532.
- Schneider, D. L., Fluckiger, H. B. and Manes, J. D., 1974.  
Vitamin K<sub>1</sub> content of infant formula products.  
*Pediatrics*, **53**, 273-275.
- Schwarz, K., 1971.  
Tin as an essential growth factor for rats. In: *Newer Trace elements in Nutrition*. Edited by W. Mertz and W. E. Cornatzer, p. 313.  
New York, Marcel Dekker.
- Scott, P. H., Berger, H. M., Kenward, C., Scott, P. and Wharton, B. A., 1975.  
Effect of gestational age and intrauterine nutrition on plasma transferrin and iron in the newborn.  
*Archives of Disease in Childhood*, **50**, 796-793.
- Seelig, M. S., 1971.  
Human requirements of magnesium factors that increase needs.  
*Proceedings of the 1st International Symposium on Magnesium Deficit in Human Pathology*. Edited by J. Durlach, p. 11.  
Vittel, France, SGEMV.
- Sivasubramanian, K. N. and Henkin, R. I., 1978.  
Behavioural and dermatologic changes and low serum zinc and copper concentrations in two premature infants after parenteral alimentation.  
*Journal of Pediatrics*, **93**, 847-851.
- Southgate, D. A. T. and Barrett, I. M., 1966.  
The intake and excretion of calorific constituents of milk by babies.  
*British Journal of Nutrition*, **20**, 363-372.
- Southgate, D. A. T., Widdowson, E. M., Smits, B. J., Cooke, W. T., Walker, C. H. M. and Mathers, N. P., 1969.  
Absorption and excretion of calcium and fat by young infants.  
*Lancet*, **1**, 487-489.
- Southgate, D. A. T. and Durnin, J. V. G. A., 1970.  
Calorie conversion factors. An experimental reassessment of the factors used in the calculation of the energy value of human diets.  
*British Journal of Nutrition*, **24**, 517-535.
- Statutory Instruments, 1960.  
The skimmed milk with non-milk fat regulations, 1960. (S. I. 1960, No. 2331).  
London, HMSO.
- Statutory Instruments, 1970.  
Labelling of Food Regulations, 1970. (S. I. 1970, No. 400).  
London, HMSO.
- Statutory Instruments, 1978.  
The Antioxidants in Food Regulations, 1978. (S. I. 1978, No. 105).  
London, HMSO.

Statutory Instruments, 1979.

Lead in Food Regulations (S. I. 1979, No. 1254)  
London, HMSO

Stimmler, L., Snodgrass, G. J. A. I. and Jaffe, E., 1973.

Enamel hypoplasia of the teeth associated with neonatal tetany.  
*Lancet*, **2**, 1085-1086.

Sunderland, R. and Emery, J. L., 1979.

Apparent disappearance of hypernatraemic dehydration from infant deaths in Sheffield.  
*British Medical Journal*, **3**, 575-576.

Suttle, N. F., 1974.

Recent studies of the copper - molybdenum antagonism.  
*Proceedings of the Nutrition Society*, **33**, 299-305.

Sutton, A. and Barltrop, D., 1973.

Absorption, accretion and endogenous faecal excretion of calcium by the newborn infant.  
*Nature*, **242**, 265.

Svennerholm, L., Alling, C., Bruce, A., Karlsson, I. and Sapia, O., 1972.

Effects on offspring of maternal malnutrition in the rat.

In: *Lipids, Malnutrition and the Developing Brain*. Edited by K. Elliott and J. Knight, p. 141.  
Amsterdam, Elsevier-Excerpta Medica.

Taylor, B., Norman, A. P., Orgel, H. A., Turner, M. W., Stokes, C. R. and Soothill, J. F., 1973.

Transient IgA deficiency and pathogenesis of infantile atopy.  
*Lancet*, **2**, 111-113.

The Royal Society, 1972.

Report of the Subcommittee on Metrication of the British National Committee for Nutritional Sciences.

Cambridge, University Printing House.

Theuer, R. C., Martin, W. H., Wallander, J. F. and Sarett, H. P., 1973.

Effect of processing on availability of iron salts in liquid infant formula products. Experimental milk-based formulas.

*Journal of Agricultural and Food Chemistry*, **21**, 482-485.

Thodenius, K., 1974.

Renal control of sodium homeostasis in infancy.

*Acta Paediatrica Scandinavica, Supplement* 253, 1-28.

Thompson, S. Y., Henry, K. M. and Kon, S. K., 1964.

Factors affecting the concentration of vitamins in milk. I. Effect of breed, season and geographical location on fat-soluble vitamins.

*Journal of Dairy Research*, **31**, 1-25.

Tipton, I. H., 1960.

Distribution of trace metals in the human body.

In: *Metal-Binding in Medicine*. Edited by M. J. Seven, p. 27.

Philadelphia, Lippincott.

Tomarelli, R. M., Meyer, B. J., Weaber, J. R. and Bernhart, F. W., 1968.

Effect of positional distribution on the absorption of the fatty acids of human milk and infant formulas.

*Journal of Nutrition*, **95**, 583-590.



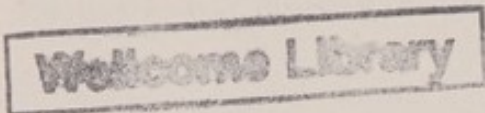
- Tripp, J. H., Wilmers, M. J. and Wharton, B. A., 1977.  
Gastroenteritis: a continuing problem of child health in Britain.  
*Lancet*, **2**, 233-236.
- Tsang, R. C., 1972.  
Neonatal magnesium disturbances.  
*American Journal of Diseases of Children*, **124**, 282-293.
- Tudvad, F., McNamara, H. and Barnett, H. L., 1954.  
Renal response of premature infants to administration of bicarbonate and potassium.  
*Pediatrics*, **13**, 4-16.
- Underwood, B. A., Hepner, R. and Abdullah, H., 1970.  
Protein, lipid and fatty acids of human milk from Pakistani women during prolonged periods of lactation.  
*American Journal of Clinical Nutrition*, **23**, 400-407.
- Underwood, E. J., 1971.  
*Trace elements in human and animal nutrition*, 3rd. edition.  
London, Academic Press.
- Van Campen, D., 1974.  
Regulation of iron absorption.  
*Federation Proceedings*, **33**, 100-105.
- Vaughan, O. W. and Filer, L. J. Jr., 1960.  
The enhancing action of certain carbohydrates on the intestinal absorption of calcium in the rat.  
*Journal of Nutrition*, **71**, 10-14.
- Watney, P. J. and Rudd, B. T., 1974.  
Calcium metabolism in pregnancy, and in the new born.  
*Journal of Obstetrics and Gynaecology, British Commonwealth*, **81**, 210-219.
- Watney, P. M. J., Chance, G. W., Scott, P. and Thompson, J. M., 1971.  
Maternal factors in neonatal hypocalcaemia: a study in three ethnic groups.  
*British Medical Journal*, **2**, 432-436.
- Whalley, P. and Walker-Smith, J. A., 1977.  
Hypernatraemia and gastro-enteritis.  
*Lancet*, **1**, 51-52.
- Wiatrowski, E., Kramer, L., Osis, D. and Spencer, H., 1975.  
Dietary fluoride intake of infants.  
*Pediatrics*, **55**, 517-522.
- Widdowson, E. M., 1965.  
Absorption and excretion of fat, nitrogen and minerals from "filled" milks by babies one week old.  
*Lancet*, **2**, 1099-1105.
- Widdowson, E. M., 1969.  
Trace elements in human development.  
In: *Mineral metabolism in paediatrics*. Edited by D. Barltrop and W. L. Burland, p. 85.  
Oxford, Blackwell.
- Widdowson, E. M., 1973.  
Composition of infant foods in Britain and the EEC. In: *Nutritional problems in a changing world*.  
Edited by D. Hollingsworth and M. Russell, p. 101.  
London, Applied Science Publishers Ltd.

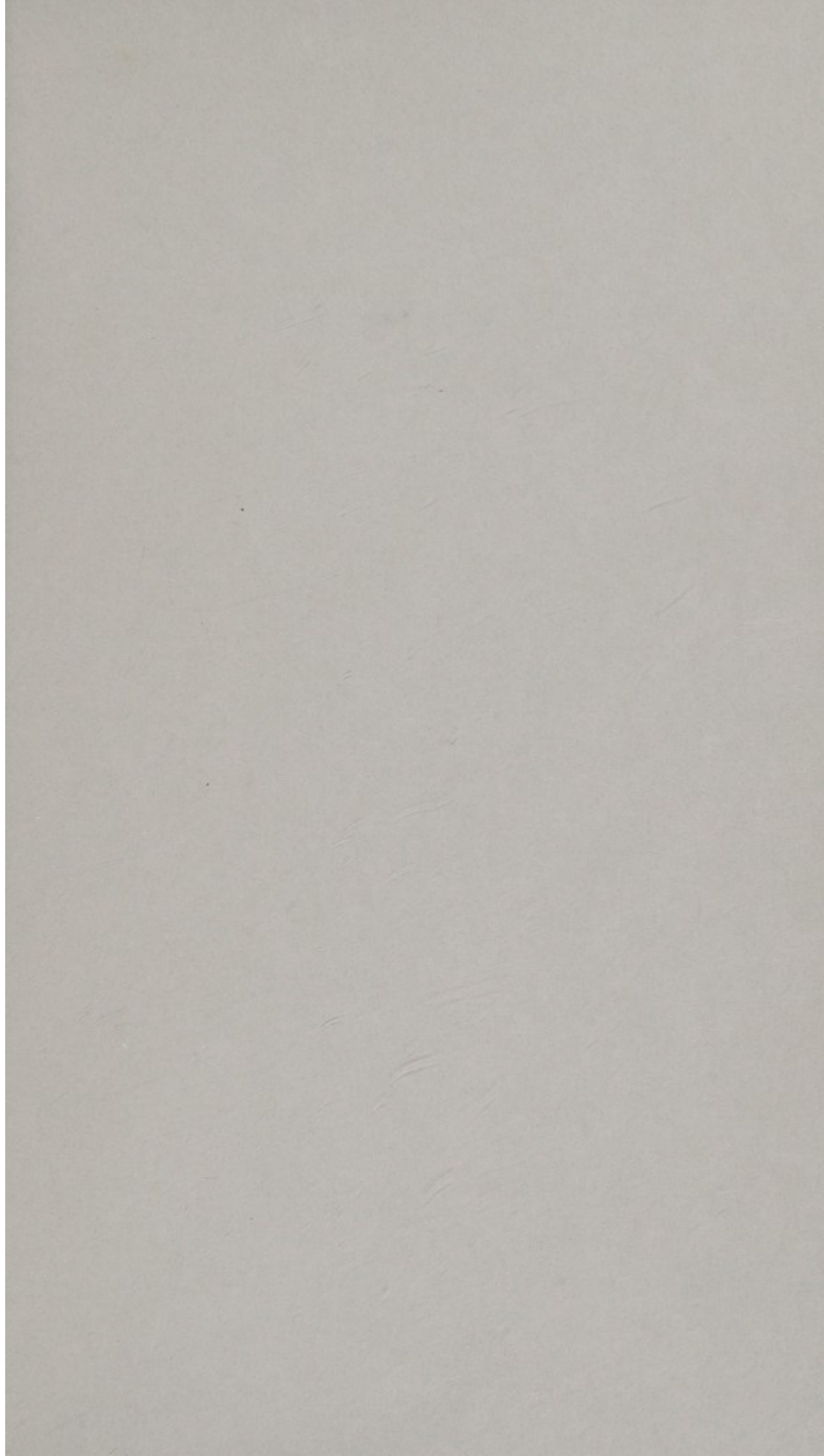
- Widdowson, E. M., Chan, H., Harrison, G. E. and Milner, R. D. G., 1972.  
Accumulation of Cu, Zn, Mn, Cr and Co in the human liver before birth.  
*Biology of the Neonate*, **20**, 360-367.
- Widdowson, E. M., Dauncey, M. J., Gairdner, D. M. T., Jonxis, J. H. P. and Pelikan-Filipkova, M., 1975.  
Body fat of British and Dutch infants.  
*British Medical Journal*, **1**, 653-655.
- Widdowson, E. M. and Dickerson, J. W. T., 1964.  
Chemical composition of the body. In: *Mineral Metabolism*. Edited by C. L. Comar and F. Bronner, p. 1.  
New York, Academic Press.
- Widdowson, E. M., McCance, R. A., Harrison, G. E. and Sutton, A., 1963.  
Effect of giving phosphate supplements to breast-fed babies on absorption and excretion of calcium, strontium, magnesium and phosphorus.  
*Lancet*, **2**, 1250-1251.
- Widdowson, E. M. and Spray, C. M., 1951.  
Chemical development in utero.  
*Archives of Disease in Childhood*, **26**, 205-214.
- Widdowson, E. M., Southgate, D. A. T. and Schutz, Y., 1974.  
Comparison of dried milk preparations for babies on sale in 7 European countries. I. Protein, fat, carbohydrate and inorganic constituents.  
*Archives of Disease in Childhood*, **49**, 867-873.
- Wilkinson, A. W., 1973.  
Some aspects of renal function in the newborn.  
*Journal of Pediatric Surgery*, **8**, 103-116.
- Williams, M. L., Rose, C. S., Morrow, G. III, Sloan, S. E. and Barnes, L. A., 1970.  
Calcium and fat absorption in neonatal period.  
*American Journal of Clinical Nutrition*, **23**, 1322-1330.
- Williams, M. L., Shott, R. J., O'Neal, P. L. and Oski, F. A., 1975.  
Role of dietary iron and fat on vitamin E deficiency anaemia of infancy.  
*New England Journal of Medicine*, **292**, 887-890.
- Wilson, J. F., Lahey, M. E. and Heiner, D. C., 1974.  
Studies on iron metabolism.  
*Pediatrics*, **84**, 335-344.
- Witting, L. A., 1972.  
The role of polyunsaturated fatty acids in determining vitamin E requirement.  
*Annals of the New York Academy of Sciences*, **203**, 192-193.
- Woodruff, C. W., Bailey, M. C., Davis, J. T., Rogers, N. and Coniglio, J. G., 1964.  
Serum lipids in breast-fed infants and in infants fed evaporated milk.  
*American Journal of Clinical Nutrition*, **14**, 83-90.
- Woodruff, C. W., Wright, S. W. and Wright, R. P., 1972.  
The rôle of fresh cows' milk in iron deficiency.  
*American Journal of Diseases of Children*, **124**, 26-30.
- Woodruff, C. W., Latham, C. and McDavid, S., 1977.  
Iron nutrition in the breast-fed infant.  
*Journal of Pediatrics*, **90**, 36-38.



Young, T., 1761.  
De Lacte.  
Edinburgh.

Ziegler, E. E. and Fomon, S. J., 1971.  
Fluid intake, renal solute load, and water balance in infancy.  
*Journal of Pediatrics*, 78, 561-568.







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