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PHYSIOLOGICAL DEVELOPMENT OF THE INFANT AND ITS IMPLICATIONS FOR COMPLEMENTARY FEEDING

by

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The implications of complementary feeding are considered in relation to the physiological development and nutritional requirements of the infant. From the standpoint of nutritional needs and physiological maturation, the provision of foods other than breast milk before about four months of age is unnecessary and may also be harmful. On the other hand, most infants require some complementary feeding by about six months of age. The period between four and six months can be used as a period of training and adaptation to semi-solid food. There are a number of known disadvantages and risks involved in too early complementary feeding including interference with the infant's sucking reflex, diminishment of the frequency and intensity of sucking with a reduction in breast-milk production, hindrance of iron absorption from breast milk, and increased risk of diarrhoeal diseases. With many complementary foods, including undiluted cow's milk, there is a risk of a water deficit with a resultant hyperosmolarity and hypernatraemia, leading to lethargy, convulsions and even residual brain damage. Other possible long-term implications include the development of obesity, hypertension and arteriosclerosis in later life. The paper points out that the decision when to start complementary feeding depends not only on age but also on the developmental stage of the infant, the type of food available, and the sanitary conditions in which the food is prepared and administered.

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INTRODUCTION

1. During the period of intrauterine life the fetus is fed "blood to blood" through the placenta. The placenta extracts from the mother's blood all required nutrients which go directly into the fetal circulation in a form that can be immediately utilized by its metabolic processes. Thus glucose is the main source of energy and free amino acids are used for protein synthesis.

2. There is very little in the way of metabolic byproducts and whatever is produced goes back into the mother's circulation. With this mechanism of parenteral nutrition the fetus does not need to ingest, digest and absorb food; nor does it need an excretory system to clear its body of metabolic wastes. The gastrointestinal tract and renal functions start to develop progressively prior to birth, in preparation for the day when they will be needed.

3. There is evidence that late in pregnancy the fetus demonstrates swallowing movements and takes in amniotic fluid; this has very little, if any, nutritional significance, though it is of importance for the anatomical and functional development of the fetal gastrointestinal system. Similarly, the fetus produces and excretes urine, which contributes to the maintenance of amniotic fluid, and acts on the development of the kidneys even though they are not yet required.

4. The situation changes suddenly and radically at birth, after which the infant must take food by mouth, digest and absorb nutrients, and requires functional kidneys to excrete metabolic wastes and maintain water and electrolyte homeostasis. However, since neither of the two systems is at that time fully developed, the margin of tolerance for water, overall solute load and specific solutes is very narrow compared to the older infant and young child. Because of the inability of the kidneys to concentrate urine at birth and for several months thereafter, the neonate and young infant require food with a higher water content than does the older infant in order to be able to secrete a comparable solute load. The newborn passes from a practically sterile environment to a heavily contaminated one in which even the food ingested may be a source of infection.

5. The process of adaptation to these drastic changes takes place during the first few months of extrauterine life. This is a period during which the infant is also growing very rapidly and has therefore very high nutritional requirements. Both the rooting reflex and the extrusion reflex (vide infra), present at birth and active through the first three months of life, prime the infant to receive only liquid nourishment, particularly breast milk. Regurgitation of other foods, if given at this time, is common.

6. In deciding on appropriate infant feeding practices during the first few months of life, it is necessary, therefore, to consider nutritional needs and degree of functional maturation, particularly in regard to the infant's utilization of foods, the excretory mechanisms, and defence against infections.

7. This paper reviews the process of development of the gastrointestinal tract and renal functions during early extrauterine life and the nutritional needs of infants; and considers infant-feeding practices, particularly complementary feeding, in the light of these two factors.

DEVELOPMENT OF THE GASTROINTESTINAL TRACT FUNCTIONS

Food ingestion

8. At birth the normal infant is able to suck from the mother's breast, conduct the milk thus obtained to the back of the mouth and swallow it. The infant can do this for five to ten minutes continuously while breathing normally. The sucking and swallowing functions are vital for the newborn and the infant during the first months of life. They are achieved by a special morphological configuration of the mouth, with, in particular, a proportionately longer soft palate than is found later in life, and by the sucking and swallowing reflexes, which direct a series of coordinated movements of the lips, cheeks, tongue and pharynx.

9. If solid or semi-solid food were to be placed in the infant's mouth, it would normally be rejected vigorously by the action of the extrusion reflex, another normal reflex of the young infant. It is only at four to six months of age, when the tongue thrust or extrusion reflex is normally no longer present, that the infant is able to accept semi-solid foods; hence the food can be transported to the rear of the mouth and swallowed.[1] The series of movements needed for this purpose are different from those needed for sucking and swallowing liquids. Later, at seven to nine months of age, rhythmic biting movements start to appear at the same time as the first teeth are erupting; mastication has begun.

10. For the first four to six months of life the normal infant is thus at a stage of functional development that allows the acceptance of an essentially liquid diet. This is a period of transition between the parenteral nutrition of the fetus _in utero_ and the mixed, mainly solid, diet of later life. While a young infant can be forced to take soft semi-solid foods from the first days after birth, for example by a mother who learns how to utilize the infant's sucking movements to feed such foods, this cannot be considered a normal situation.

Food digestion

11. Carbohydrates. The process of digestion of foods starts in the mouth; during mastication foods are mixed with saliva allowing the action of amylase to start the digestion of starches. Although amylase has been found in infant saliva, no digestion of carbohydrates takes place in the mouth or oesophagus during the first months of life.

12. It is in the proximal small intestine that carbohydrates are mainly digested. Polysaccharides, like starches, are degraded into mono- and disaccharides, primarily by the action of delta-amylase secreted by the pancreas. Glucoamylase secreted by the intestinal mucosa may also contribute to the digestion of starches, but it acts primarily on oligosaccharides and some disaccharides. The small intestine's mucosa also secrete disaccharidases which hydrolyse disaccharides into monosaccharides, the only form in which carbohydrates can be absorbed.

13. It has been found that infants born at term have approximately 10% of adult amylase activity in their small intestine,[2] and this seems to be mainly glucoamylase activity. Present information indicates that pancreatic amylase is not secreted during the first three months of life; it has been found to be present at only very low levels, or still absent altogether, up to six months of age.[3]

14. There is, however, some evidence that infants can digest starches before three months of age. This is probably due to the activity of glucoamylase, which is not normally active at this time, but which is activated by the presence and nature of the substance or substrate on which the enzyme acts.[4] It is also possible that pancreatic amylase could be produced as a reaction to the presence of starches in the small intestine, although this has not been proved. In any case, a process of adaptation is required for the young infant to be able to digest starches. This can take days or weeks and might explain the frequency with which gastrointestinal disturbances, particularly diarrhoea, are observed in small infants fed starch-containing foods. It has also been suggested that undigested starches may interfere with the absorption of other nutrients and result in failure to thrive in infants fed diets containing a large proportion of starches.[5]

15. Contrary to the evident immaturity of the infant's system for the digestion and utilization of starches during the first months of life, the activity of the disaccharidases is fully developed at birth. Both delta-glucosidase, which hydrolyses sucrose and maltose, and beta-galactosidase, which hydrolyses lactose, are present at birth at the same levels of activity as those found in older infants.[6] No problem exists, therefore, for the digestion and utilization of milk sugar.

16. Proteins. The gastric secretion of hydrochloric acid and pepsin is already well developed in the newborn at term; concentrations are low, however, and increase progressively during the first four months of life.[7,8] In any case, the digestion of proteins takes place mainly in the small intestine, where proteolytic activity in the newborn has reached the same concentration as in adults.[9] Thus, while the young infant may have some difficulty with proteins like casein for which gastric activity can be important to initiate digestion, the infant's capacity to digest proteins is otherwise fully developed at birth. Nevertheless, very high protein intake should be avoided, particularly in the pre-term and very young infant, in whom an excessive renal solute load may produce acid-base imbalances and metabolic acidosis.

17. Another problem related to the utilization of proteins by the young infant is the permeability of the intestinal mucosa to large molecules. In older infants, as in adults, proteins are absorbed as amino acids and small peptides. Most of the latter are further digested during their passage through the mucosa and it is mainly the free amino acids which enter the circulation. Large molecules, which can act as antigens, do not normally cross the intestinal mucosa. During the neonatal period, however, and for a variable period thereafter, the infant is able to absorb intact protein molecules.[10] This has been proved by the absorption of antibodies and by the immunological response to protein antigens administered orally.

18. This characteristic of the young infant seems to be the mechanism by which an allergic reaction to cow's milk sometimes develops in children. The implications of the mechanism in the development of other food allergies is not clear, but should be kept in mind where the feeding of young infants is concerned.

19. Fats. As mentioned above, glucose is the main source of energy for fetal development during the intrauterine period. After birth, however, dietary fats become an important source of energy. Forty to 50% of energy in human milk is in the form of fats. A drastic adjustment in energy metabolism is therefore required after birth, starting with the digestion and absorption of fats.

20. In older infants and adults, dietary fats are first hydrolysed, mainly by the activity of the pancreatic lipases in the small intestine. The products of lipolysis are then solubilized for absorption by the action of the bile salts. In the newborn at term the pancreatic and hepatic functions are not yet fully developed and the concentrations of both pancreatic lipase and bile salts are very low.[11,12]

21. It has been observed, however, that there is an adequate absorption of fats, particularly those from human milk in young infants. This is surprising considering that milk fat droplets are particularly resistant to the lipolytic activity of pancreatic lipases because they are enveloped by a layer of phospholipids and proteins. It is known that in young infants fat digestion and absorption are enhanced by the action of lingual lipases[13] and by the action of lipases contained in human milk.[14] Lingual lipases are secreted by papillae of the posterior part of the tongue; they start to act in the stomach, and the products of lipolysis (fatty acids and monoglycerides) contribute to the emulsification of the mixture compensating for the low bile-salt content. This mechanism of preduodenal lipolysis, important in the young infant, is further complemented by the lipase contained in human milk (bile-salt stimulated lipase), which also plays an important role in fat digestion and absorption in early infancy. The human-milk lipase also has esterase activity, which is important for the utilization of vitamin A that is present in milk in the form of retinol esters.

22. In spite of the immaturity of the pancreatic and hepatic functions, the young infant is thus well equipped to make use of human milk fat, which provides close to 50% of energy requirements, as well as other important fat-soluble components of human milk. These compensatory, or complementary, mechanisms for fat utilization by young infants are less efficient when cow's milk fat or other fats are introduced into their diet.[15]

23. Vitamins and minerals. No major problems seem to exist in the utilization of dietary vitamins and minerals in early life. However, the subject has not been studied as much as the digestion and utilization of the macronutrients already discussed. The absorption of fat-soluble vitamins is closely linked to fat absorption.

24. For vitamin A in particular, not enough is known about the utilization by young infants of the different forms in which this vitamin or its precursors can occur in foods. The particularly high absorption of vitamin A in human milk has already been mentioned.

25. A similar situation exists for iron, the absorption of which is higher in infants than in older children and adults. This seems to be related to a greater need for the mineral in early life. In addition, the bioavailability of iron from human milk is particularly high; it is much higher than the iron from cow's milk or of iron preparations added to foods.[16] The exact mechanism that enhances the availability of iron for breast-fed infants is not known. It has been observed, however, that the high bioavailability of human-milk iron decreases drastically when solid complementary foods of vegetable origin are given to the breast-fed infant. This situation has been confirmed experimentally by measuring, in adults, the iron absorption from human milk alone or when fed together with a common complementary infant food (strained pears). The absorption of iron was found to be 23.8% and 5.7% respectively.[17]

26. Water and electrolytes. The permeability of the intestinal mucosa to water and electrolytes is higher in infants than later in life. This is of no significance under normal conditions, but becomes important in situations of high osmolarity in the intestinal content. Under these circumstances the infant tends to develop water and electrolyte imbalances more easily than later in life. The implications of this situation for infant feeding should be borne in mind (see paragraph 30).

EXCRETORY SYSTEM

27. The maintenance of the amount and composition of body fluids and the excretion of metabolic wastes are vital functions of the kidneys. *In utero* urine formation starts early in the development of the fetus, that is to say by the ninth to tenth week of gestation. Excretion of urine at this stage plays a role in the maintenance of amniotic fluid and in the embryogenesis of the urinary system. The regulatory and excretory functions of the kidneys are minimal before birth, however, as the task of maintaining fetal homeostasis is carried out by the placenta. Metabolic wastes are practically nil, since metabolism of the fetus is fundamentally anabolic; whatever waste there is passes through the placenta into the maternal circulation. This is confirmed by the fact that infants born with renal agenesis do not manifest any renal insufficiency at birth.

28. At birth the kidneys are performing all their functions but at a low level. They are adapted to the normal situation of the newborn who will continue with a predominantly anabolic metabolism provided that a balanced, fully utilizable, low-residue food, namely breast milk, continues to be fed. The kidneys' functional capability will quickly increase during the first few months of life. This is illustrated by the rapid extrauterine growth of the organs, from 12.5 g at birth to 20 g per kidney at 13 months of age.

29. Functionally the kidneys of the newborn are characterized by a low glomerular filtration rate and a low concentration capability.[18] They function very efficiently as a mechanism for water conservation to provide a defence against dehydration. They have no problem in eliminating the low metabolic residues of a breast-fed infant.

30. The system may fail, however, when the intake of water is markedly reduced or the intake of solutes markedly increased. Because of the very different nutritional requirements of the human infant compared to those of the calf, the sudden introduction of cow's milk into the young infant's diet may lead to hyperosmolarity with hypernatraemia which, if not checked, may result in lethargy, convulsions and even central nervous-system damage. A cow's-milk diet for a young infant can lead to a water deficit of 80 ml/day. The situation becomes particularly critical when there are extrarenal water losses such as occur with copious sweating.

31. In regard to acid-base regulation, the kidneys of the young infant have a low capability to eliminate hydrogen ions,[19] and hence the greater susceptibility of the infant for developing acidosis. A clear example of how the infant's kidneys adapt their functional capacity to demand is phosphate excretion. The young infant's kidneys normally function with a low phosphate intake, as was the situation *in utero*, and should

continue provided the infant is breast-fed. However, when the infant is put on a high phosphate diet, cow's milk for instance, the kidneys have to adjust to another level of function. They usually respond to this demand, but it takes some time to make the adjustment. In the meantime the infant may develop a transitory hyperphosphataemia, as a result of both renal immaturity and functional hypoparathyroidism; this situation may be associated with hypocalcaemia and neonatal tetany.[20]

32. The relative immaturity of the renal system of the newborn seems to be due only to the fact that the level of function provided is in accordance with the expected demand. The kidneys subsequently mature very rapidly during the first few months of life and they have the capacity to adapt to significant variations in diet. Thus, starting at about four months, the solute load resulting from the metabolism of newly introduced foods is acceptable, and by six months of age, the swallowing of fluids offered by cup has begun to be developed. In fact, progressive modifications in dietary intake, with increments in urea and other solutes to be excreted, act as a stimulus to the kidneys for attaining higher functional levels.

33. However, the system may be overburdened more easily during the early months than later in life by situations of stress like disease, dehydration and sudden or too drastic dietary changes such as the inclusion of foods with high sodium (minerals) or solute loads (proteins) which would require water supplements (see Table 1, parts A and B).

NUTRITIONAL REQUIREMENTS

34. The first few months of life is a period of very rapid growth, with the weight of a normal infant doubling by four months of age. Energy and nutrients are needed not only for maintenance of bodily functions and activity, but also in a large proportion for tissue deposition. The nutritional requirements of the infant are consequently different from those of older children and adults, both quantitatively and qualitatively.

35. Quantitatively, for example, the requirements for both energy and protein during the first month of life are, on a per kilogram basis, about three times those of the adult. There are also important qualitative differences, related either to actual needs or to the particular physiological characteristics of the infant.

36. With regard to proteins, the requirements of infants for essential amino acids are proportionately much higher than in older children and adults.[21,22] It would therefore be very difficult, if not impossible, to satisfy their nitrogen needs with proteins of low biological value. Although fats as such are not required, except for very small amounts of essential fatty acids, they are extremely important for the infant as concentrated sources of energy, allowing the high energy intake required within a reasonable volume of food. The requirements for minerals are particularly critical at this age; iron and calcium, needed for haemoglobin formation and bone calcification, are notable examples.

37. There are more than 50 nutrients that are known to be needed by human beings, although information on the requirements in respect of more than half of them is lacking. For most nutrients there is not only a minimum level of intake below which deficiency occurs, but also a maximum level above which their intake could have undesirable consequences. While the range between these minimum and maximum desirable levels is usually quite wide and allows for a large safety margin in the variation of intake, for some it is quite narrow, particularly in the case of energy. Energy intake levels slightly below those required will result in a deficiency while those above will produce obesity.

38. A very delicate balance of energy and of a large number of nutrients is therefore needed for proper infant nutrition and health. Fortunately, in deciding about an adequate diet, there is no need to consider each individual nutrient, but rather the foods to be provided. Where infants are concerned, it is recognized that breast milk is a complete and perfectly balanced mixture of all required nutrients. If the infant's energy needs are satisified with breast milk, all other nutritional requirements will also be met.

TABLE 1. NUTRIENT CONTENT OF SOME COMPLEMENTARY FOODS FOR INFANTS

A. Macronutrients

(Average content per 100 g)

PRODUCT[1]	COUNTRY	PREPARATION	ENERGY		WATER	PROTEIN	FAT		CARBOHYDRATES		
			kcal	kJ			Total	PUFA[2]	Total	Fibre	Starch
Carrot purée	Sweden	industrial	50	200	77.6	1.0	2.0	0.12	7.0	0.77	1.17
Apple purée	England	industrial	59	253	*	0.2	ND	ND	15.6	*	*
Rice/milk gruel(powder)	Fed.Rep.of Germany	industrial	423	1795	*	10.7	8.9	1.3	75.0	0.1	33.6
Mixed cereals	Netherlands	industrial	354	1505	*	10.0	2.0	*	74.0	6.5	*
High protein cereal**	USA	industrial	360	1512	6.8	35.2	4.6	*	44.3	2.4	*
Chicken/vegetables/ potatoes	Sweden	industrial	75	320	*	3.0	3.0	*	8.5	*	*
Sweet potatoes	Jamaica	home made	119	477	70.6	1.7	0.4	*	26.3	0.7	*
Green beans	Turkey	home made	32	130	90.1	1.9	0.2	0.07	6.1	1.0	3.5
Papaya	Jamaica	home made	39	160	88.7	0.6	0.1	*	10.0	0.5	*
Peach	Turkey	home made	38	160	89.1	0.6	0.1	0.05	9.7	0.6	0.1
Fruit***	USA	industrial	85	357	78.2	0.4	0.2	*	20.4	0.5	*
Rice flower/milk/sugar	Turkey	home made	140	586	31.4	2.8	1.2	0.07	28.8	0.07	19.3
Corn flower/water	United Rep. Tanzania	home made	73	304	2.4	1.6	0.5	0.04	15.4	0.14	12.8
Rice/oil/butter/water	India	home made	141	591	3.1	1.9	5.5	1.58	20.3	0.05	20.3
Almond/butter/honey/ water	Saudi Arabia	home made	562	2350	11.2	9.5	47.1	6.01	30.4	1.3	9.8
Wheat bread/mint tea	Morocco	home made	288	1210	33.1	8.6	3.8	0.48	53.0	0.2	53.0

* No information available. ** Average values of 3 products. *** Average values of 33 products. ND = none detectable.

1 References as below.

2 PUFA = polyunsaturated fatty acids.

TABLE 1. NUTRIENT CONTENT OF SOME COMPLEMENTARY FOODS FOR INFANTS

B. Minerals

(Average content per 100 g)

PRODUCT[1]	ASH	CALCIUM mg	PHOSPHORUS mg	POTASSIUM mg	SODIUM mg	IRON mg	COPPER mg	MAGNESIUM mg	ZINC mg
Carrot purée	0.7	35	30	100	50	0.6	0.06	10	0.20
Apple purée	*	12	5	107	17	0.4	*	*	*
Rice/milk gruel(powder)	*	440	230	430	130	5.0	*	20	*
Mixed cereals	*	50	280	280	260	4.2	*	80	*
High protein cereal**	6.7	811	849	1 492	68	80.0	0.1	*	*
Chicken/vegetables/ potatoes	*	20	30	170	140	0.7	0.05	10	0.30
Sweet potatoes	1.0	32	47	243	10	0.7	*	75	*
Green beans	0.7	56	44	243	7	0.8	0.13	32	0.80
Papaya	0.6	20	16	234	3	0.3	0.01	8	0.40
Peach	0.5	9	19	202	1	0.5	*	10	0.15
Fruit***	0.3	8	12	79	17	0.4	0.06	*	*
Rice flower/milk/sugar	0.4	45	53	76	16	0.2	0.01	9	0.50
Corn flower/water	0.1	1	33	ND	ND	0.4	0.03	17	0.28
Rice/oil/butter/water	0.2	15	50	38	53	7.0	0.11	7	0.46
Almond/butter/honey/ water	1.9	118	254	403	131	2.5	*	2	1.65
Wheat bread/mint tea	1.5	28	94	125	406	5.3	0.13	104	04.49

* No information available. ** Average values of 3 products. *** Average values of 33 products. ND = none detectable.

1 Countries and preparation as above, references as below.

TABLE 1. NUTRIENT CONTENT OF SOME COMPLEMENTARY FOODS FOR INFANTS

C. Vitamins

(Average content per 100 g)

PRODUCT[1]	RETINOL eqv.mg	VIT.D µg	VIT.E mg	THIAMIN mg	RIBOFLAVIN mg	NIACIN mg	VIT.B6 mg	VIT.B12 µg	FOLIC ACID µg	VIT.C mg	REFERENCES
Carrot purée	1.00	ND	*	0.03	0.03	0.4	*	ND	*	5	(1)
Apple purée	*	*	*	*	*	*	*	*	*	25	(2)
Rice/milk gruel (powder)	3.30	4.75	3.3	1.3	0.28	2.6	0.24	0.47	47.1	28	(3)
Mixed cereals	*	*	*	0.3	0.1	*	0.20	*	*	*	(4)
High protein cereal**	*	*	*	3.22	1.85	21.0	0.56	*	*	*	(5)
Chicken/vegetables/ potatoes	0.10	*	*	0.04	0.02	0.7	*	*	*	ND	(1)
Sweet potatoes	0.03	ND	*	0.10	0.06	0.6	0.21	ND	88.4	21	(6)
Green beans	0.06	ND	0.09	0.08	0.11	0.5	0.15	ND	27.5	19	(7)
Papaya	0.18	ND	*	0.04	0.04	0.3	0.04	ND	1.1	56	(6)
Peach	0.13	ND	ND	0.02	0.05	1.0	0.02	ND	*	7	(7)
Fruit***	0.12	*	*	0.02	0.02	0.2	0.05	0.06	0.4	6.8	(5)
Rice flower/milk/sugar	0.01	ND	0.07	0.03	0.06	0.4	0.04	ND	1.07	ND	(7)
Corn flower/water	ND	ND	ND	0.04	0.01	0.3	0.08	ND	5.3	ND	(8)
Rice/oil/butter/water	0.02	ND	0.44	0.11	ND	0.9	0.03	ND	0.9	ND	(9)
Almond/butter/honey/ water	0.17	0.25	12	0.12	0.48	1.9	0.06	ND	23	ND	(9)
Wheat bread/mint tea	ND	ND	1.8	0.27	0.15	3.0	0.26	ND	29	ND	(9)

* No information available. ** Average values of 3 products. *** Average values of 33 products. ND = none detectable.

[1] Countries and preparation as above.

References: (1) Brown, R.E. Weaning foods in developing countries. American Journal of Clinical Nutrition, 31:2066-2072 (1978)
(2) Cow & Gate Ltd., Trowbridge, England
(3) Fomon, S.J. Infant nutrition, Philadelphia, Saunders, 1967
(4) Jelliffe, E.F.P. A new look at weaning multimixes for the Caribbean - means of improving child nutrition. Jamaica, Caribbean Food and Nutrition Institute, 1971
(5) Köksal, O. Nutrition in Turkey. Ankara, UNICEF, 1977
(6) Marchione, T.J. & Helsing, E. Rethinking infant nutrition policies under changing socioeconomic conditions. University of Oslo, Institute for Nutrition Research, February 1981
(7) International Division/Scientific Department, Milupa, Ag, Friedrichsdorf, Federal Republic of Germany
(8) Nutricia Produktinformatie, Zoetermeer, Netherlands
(9) Semper Produktinfomation, Stockholm, Semper AB. June 1984

39. On this basis, and since the main purpose of this paper is to help in deciding when foods other than breast milk become necessary or are recommendable in infant feeding, only energy requirements will be considered in detail. The situation would be different in regard to infants fed with breast-milk substitutes and for whom some nutrients would have to be added even though total energy intake was adequate. This is the case, for example, for vitamin C and iron, and also for vitamin D in conditions of low exposure to sunlight (see Table 1, parts B and C).

Energy requirements of infants

40. Energy requirements can be defined as the level of energy intake from food that will balance energy expenditure in healthy individuals. Energy expenditure includes the basic metabolic rate, the energy expended in activity, and the energy cost of food utilization. In the case of pregnant and lactating women, the energy cost of pregnancy and lactation has to be added, and in the case of children, the energy required for growth.

41. Energy requirements should in principle be determined by accurate measurements of all the above-indicated components, which can usually be done in the case of older children and adults. No reliable information is available on the energy required for adequate growth and physical activity of infants. It is recognized, however, that healthy infants, growing within accepted standards, are presumably in energy balance. The energy intake of healthy infants has therefore been used as the basis for establishing energy requirements for infants.

42. For the estimation of energy requirements of infants under six months of age, the FAO/WHO Ad Hoc Expert Committee on Energy and Protein Requirements[23] used data on the intake of infants fed with human milk by bottle;[24] for infants in the second half of their first year of life, data were used on healthy children from the United States of America and the United Kingdom fed on a mixed diet.[25] The limitations of the information were recognized but it was the best available; the Committee recommended that additional data be collected.

43. The recommendations of the 1971 Committee, which have been the ones most widely used internationally up to now, were for 120 kcal (0.502 MJ) per kg per day for infants 0 to 3 months of age, decreasing progressively to 105 kcal (0.439 MJ) per kg per day for infants 9 to 12 months of age (see Table 2).

TABLE 2. ENERGY REQUIREMENTS OF INFANTS

Age in months	kcal/kg/day	MJ
0 - 3	120	0.502
3 - 6	115	0.481
6 - 9	110	0.460
9 - 12	105	0.439

44. As indicated above these figures have been used to estimate the adequacy of, or make recommendations on, the dietary intake of infants. Using these values, for example, it was estimated that the usual breast-milk secretion of healthy mothers was insufficient to satisfy the energy requirements of infants beyond three months of age.[26]

45. Another Committee, jointly sponsored by WHO, FAO and UNU, met in 1981 to review energy and protein requirements.[27] This Committee had available a much larger collection of measurements of food intake of infants from Canada, Sweden, the United Kingdom and the United States of America[28] who were healthy and growing within the WHO recommended standards. Data from developing countries were intentionally not included in order to eliminate infants frequently growing below the recommended standard, which is a situation recognized to be associated primarily with an inadequate diet and frequent infections and not due to genetic differences.[29] The results of the analysis of the data used by the 1981 Committee are interesting, and are summarized in Table 3.

TABLE 3. ENERGY INTAKE OF INFANTS

Age in months	Intake	
	kcal/kg/day	MJ
0.5	118	0.494
1 - 2	114	0.477
2 - 3	107	0.448
3 - 4	101	0.423
4 - 5	96	0.402
5 - 6	93	0.390
6 - 7	91	0.381
7 - 8	90	0.337
8 - 9	90	0.377
9 - 10	91	0.381
10 - 11	93	0.390
11 - 12	97	0.406
12	102	0.427

46. It can be seen that although the values start at a similar level to those of the recommendations of the 1971 Committee, they drop very rapidly during the first months to attain a lower level between six and ten months of age and rise again thereafter. This U-shaped curve is very different from the progressively decreasing line followed by the values of the 1971 Committee. It is considered to be more accurate however, and probably related to a rapid decline in need for energy for growth. In contrast, energy expenditure in activity, low at the beginning, increases progressively and becomes of greater significance during the latter part of the first year.

47. The differences between these observed intake values and the recommendations of the 1971 Committee are quite wide, particularly from three to nine months of age. This is a critical period during which the weaning process starts.

48. The practical significance of the new information, used as the basis for the recommendations of the 1981 Committee, is enormous. It explains observations indicating that under natural conditions, where there is neither severe malnutrition, health problems, nor other reasons of physiological or sociopsychological origin reducing a mother's milk production, breast milk alone satisfies the energy requirements of infants for at least the first four months of life and frequently up to six months.[30]

49. As mentioned earlier, if the energy requirements of an infant are satisfied with breast milk, there should be no problem with proteins and all other essential nutrients. Exceptions to this rule are infants with very low birth weight, who may need iron supplementation, and infants born of mothers with specific vitamin and mineral deficiencies. In the latter case, the milk of the mother may have low values of a given nutrient and the infant may have to receive it as a supplement.

50. The situation is different for infants fed with breast-milk substitutes, who would normally require early supplementation with vitamin C; with iron when the breast-milk substitute used is not enriched with this mineral; and with vitamin D when, because of environmental or other reasons, infants do not receive sufficient sunlight.

PROTECTIVE FACTORS OF HUMAN MILK

51. Human milk contains a variety of protective substances such as Lactobacillus bifidus and antistaphylococcal factors; lysozyme; lactoferrin; components of the complement system; immunoglobulins A, G and M; lymphocytes; neutrophiles; and macrophages. There are other substances in human milk, such as lipids, which may have an antiviral activity.[31] Receptor-like carbohydrates may also be important in preventing adherence of bacteria to the intestinal mucosa.[32]

52. The main soluble component of the immune system in human milk is the secretory immunoglobulin A (SIgA). SIgA antibodies appearing in milk are produced by IgA-committed lymphocytes primed in the intestine; these lympocytes migrate to mucosal sites and, in pregnant and lactating women, also to the mammary gland.[33] The enteromammary connection assures that the breast-fed infant will receive, through the mother's milk, antibodies specifically directed against the intestinal pathogens present in the maternal environment.[34]

53. Milk SIgA antibodies may prevent the adherence of the microorganisms to the intestinal mucosa and may have bacteriostatic and neutralizing activities, in conjunction with other milk components, such as lactoferrin. Epidemiological prospective studies, in which specific milk SIgA antibodies, infant intestinal infection, and specific morbidity have been monitored, show that high levels of SIgA antibodies in milk are associated with protection from illness even in the presence of intestinal infection.[35]

54. Specific antibodies present in milk vary from one population group to another, since their induction depends on the antigens to which they are exposed. The appearance of SIgA antibodies in milk, however, does not guarantee their constant concentration or their total output in milk throughout lactation. Fluctuations of specific milk antibodies have been observed in lactating mothers followed periodically, in both developed and developing societies.[36,37]

55. Changes in the concentration of milk antibodies are independent of the content of SIgA and other antibodies, and seem to be more dramatic in women living under poor hygienic conditions where they may reach undetectable levels for long periods of time. It may be possible that the fall in concentration of antibodies is related to antigenic intestinal exposure by the lactating mother. An infection in the maternal gastrointestinal tract may interfere with the enteromammary transit of IgA-committed, primed lymphocytes, and therefore induce the disappearance of specific antibodies from the mother's milk. If, at that time, an infection by the same microorganism occurs in the breast-fed child, it is very likely to be symptomatic.

56. The importance of maternal carriage of enteropathogens becomes more obvious in the light of the above considerations. For this reason, the improvement of household hygiene, especially in regard to the food and water consumed by adults, attains as much importance as that so far given to non-contamination of weaning foods.

COMPLEMENTARY FEEDING

57. Based on physiological maturation and nutritional requirements of infants, it can be concluded that the administration of other foods to the breast-fed infant before about four months of age is usually unnecessary and may entail some risks. On the other hand, by six months of age most breast-fed infants require some complementary feeding and are fully developed functionally to cope with it.

58. When to start complementary feeding in breast-fed infants cannot be decided exclusively on the basis of age. One must also consider the developmental stage of the infant, the types of food available, and the environmental conditions and facilities to prepare and administer the food safely.

59. The developmental stage can be assessed by the infant's neuromuscular capabilities. If the infant is able to hold the head erect, starts to put his or her hands to the mouth and accepts semi-solid foods without difficulty (extrusion reflex), he or she is ready to start receiving complementary foods.

60. With regard to types of food available, it should be remembered that the weaning process, which starts with the introduction of complementary foods, has as its final objective the progressive transfer of the child from breast milk to the usual family diet. The types of food which are normally consumed at home or are easily available, and the facilities to prepare and administer them easily and safely, will also influence the decision about the best time to initiate complementary feeding. If the foods that are available for the young infant are of a very low nutritional value, or are too coarse, difficult to prepare in a soft semi-solid form, or environmental conditions favour heavy contamination, it would be preferable to delay the introduction of complementary foods until they become strictly necessary for nutritional reasons.

61. An analysis of recent data on energy requirements of the young infant indicates that, unless there are signs of severe maternal malnutrition or other physiological or psychological reasons for reduced levels of mother's milk, breast milk alone satisfies the energy requirements of the infant for at least the first four months of life, and frequently up to six months. The period between four and six months can be used as a period of training and adaptation to semi-solid foods before such foods become essential to continued growth and development.

62. Obviously growth velocity also needs to be considered. If a breast-fed infant is not growing properly and no other reason can be found for it, the need to start complementary feeding should be considered. In practice, however, there is no need to wait for growth faltering to initiate complementary feeding. As discussed above, the timely administration of such foods should first accustom the infant to new experiences so that when they become nutritionally necessary the infant will be able to take them in sufficient amounts. It should be remembered that eating, in addition to its nutritive role, has important educational and emotional implications; this holds true from very early infancy.

Complementary foods

63. Breast milk is the standard food for the human infant. Once other foods start to be given, they can be as varied as are normal family diets. What needs to be taken into consideration are their nutritional value and safety, their physical characteristics in accordance with the physiological capabilities of the infant, and their cultural, ecological and economic appropriateness.

64. From the nutritional point of view it should be remembered that complementary foods are going to progressively replace breast milk, which is a complete and balanced food. At the onset of complementary feeding, when the infant is still predominantly breast-fed, complementary foods are important primarily as an additional source of energy. At the same time, however, they should also help in satisfying the requirements of all essential nutrients to which breast milk will be making a progressively decreasing contribution.

65. Particular attention should be given to proteins, iron and vitamins A and C, nutrients that are frequently found to be deficient in the diet of young infants. It is also important when initiating complementary feeding to avoid excesses that may be detrimental by themselves or may create bad dietary habits; high sodium content or excessive total energy intake can be mentioned as examples of such problems, which will be discussed further below. The safety of complementary foods should be considered in terms of possible contamination with either microorganisms or undesirable substances.

66. While there are a number of known disadvantages or risks involved in too early complementary feeding, there are others which, although extremely difficult to prove, are highly suspect in the light of evidence that has accumulated over the years. Among these may be mentioned interference with the infant's sucking reflex; diminishment of frequency and intensity of sucking, and consequent reduction in breast milk production; hindrance of iron absorption from breast milk, particularly where cereals and vegetables are concerned; and increased risk of diarrhoeal diseases in unsanitary environments (vide infra).

67. Other than the increased risk of diarrhoeal diseases arising from contaminants in food and water, or from food left standing too long before being fed to infants, there are a number of adverse nutritional consequences of too early complementary feeding. Even while continuing breast-feeding, the addition of other foods, including breast-milk substitutes, can result in a decrease of up to 75% in iron absorption.

68. Industrially prepared products for complementary feeding of infants may be a convenience under certain circumstances if economically affordable; but appropriate complementary foods can be prepared at home in the normal manner virtually everywhere.

69. Table 1 provides a few examples of the very large number of complementary feeding products that are available commercially and in the home. Homemade foods are frequently more in accordance with the cultural and economic conditions of the family and are generally low in sodium. Public health workers have an important responsibility in guiding mothers in respect of foods to be given to the infant.

Risks of starting too early

70. It is now generally recognized that infants are not ready to receive semi-solid foods before about four months of age, nor, except under very special circumstances when mothers do not produce enough milk, are these foods necessary provided that infants are breast-fed.

71. Not very long ago it was customary, particularly in the United States of America, to start complementary feeding before one month of age with cereal preparations, strained vegetables and fruits, and eggs and meat. While this practice has been largely abandoned, it is still common to give semi-solid foods to infants before three months of age.

72. There is no question that, in terms of functional capabilities, most infants can adapt to this situation. They may at the beginning refuse the food, vomit or have loose stools, but finally they will take the food without major problems. They and their mothers quickly learn how to manage semi-solid foods, even if the reflex movements of the infant mouth are not yet ready for them. Infants' digestive enzyme production, amylases in particular, is still normally low, but the potential to react to stimuli is there and thus the production of these enzymes increases when starches or other substrates are included in the diet. The kidneys, stimulated by the presence of urea derived from excessive protein, can also react by increasing their excretory capacity.

73. The question is: is it necessary "to force the machine"? Some immediate disadvantages or risks of too early complementary feeding are recognized, and the possibilities of long-term undesirable effects are suspected, although extremely difficult to prove.

74. Among the possible immediate problems the following may be mentioned. It is now well demonstrated that the introduction of foods other than breast milk into the diet of a young infant decreases sucking frequency and intensity and that, as a consequence, the milk production of the mother decreases. Under these circumstances the food given will not be a complement to breast milk so much as a partial replacement. Since in most instances the nutritional value of the "complement" is lower than that of breast milk, the child will be at a disadvantage; the opposite of the desired intention will be achieved.

75. It has also been observed that the introduction of cereals and vegetables in particular can interfere with the absorption of breast-milk iron,[17] which is normally low in concentration but high in absorbability. This can result in iron deficiency and anaemia in view of the fact that the iron balance is extremely delicate in the young infant. A deficiency may be avoided if the cereal preparations used are enriched with iron, but this would only prevent a problem that was not there at the outset.

76. Large sections of populations in developing countries have restricted diets and live in unsanitary environments. Under these circumstances the greatest immediate risk of a too early administration of complementary foods to the breast-fed infant is diarrhoeal disease.[38]

77. Indications of an association between the early introduction of contaminated foods and intestinal infections in children have been provided in longitudinal studies done in rural Bangladesh,[39] where 41% of food and 50% of water samples were contaminated with *Escherichia coli*. The proportion of water samples that contained *E. coli* was directly associated with the child's annual rate of diarrhoea due to enterotoxigenic *E. coli*. Ambient temperatures and time of storage after food preparation were directly correlated with bacterial counts. Furthermore, the monthly rates of diarrhoea associated with enterotoxigenic *E. coli* in the community correlated directly with the environmental temperature.

78. In another study in Kenya, where complementary feeding was started at three months, *Enterobacteriaceae* were found in the feeds at a level of up to 10^4 bacteria/g. The counts increased after storage of the food for periods as short as three hours.[40]

79. Enteropathogenic microorganisms do not necessarily have to be present in weaning foods before consumption, but may gain entrance into the alimentary tract of the child at the time of feeding. For example, rotaviruses were detected in hand-washings from 79% of the attendants of Bangladesh patients hospitalized because of rotavirus-associated diarrhoea.[41] The importance of microbial contamination of hands in the genesis of diarrhoea was also demonstrated with the interruption of the transmission of Shigella simply by instituting washing procedures after defecation and before meals for family members of confirmed cases of shigellosis.[42] The quantity and quality of water may be the most important factor in determining morbidity due to diarrhoeal diseases in children under three years of age.[43,44]

Possible long-term effects of inappropriate complementary feeding

80. It is now widely recognized that too late, insufficient or otherwise inadequate complementary feeding is a major problem in the feeding of infants and the main cause of child malnutrition in developing countries. At the same time, there are a number of diseases, sometimes referred to as "diseases of affluence", which are related to inappropriate dietary practices, for example obesity, hypertension and arteriosclerosis. Although these diseases normally manifest themselves only in the adult, it is now realized that their pathogenesis is a long process to which diet in early life may well be contributing. Appropriate complementary feeding practices, therefore, are critical for the prevention of the two most prevalent types of malnutrition, undernutrition in developing countries and overnutrition in industrialized ones.

81. Infant feeding practices may have a long-term impact through two mechanisms. One is the cumulative effect of changes which, starting in early life, result in clinical evidence of morbidity only after many years. The other is by creating food habits that will maintain undesirable practices, which will finally be responsible for the problem. In practice these two mechanisms may be interrelated; thus the adult's taste for salty foods may be the result of early experiences, and therefore a learned practice, while the cumulative effect of hypernatraemia over many years contributes to the development of hypertension.

82. The possible contribution of complementary feeding of infants to the pathogenesis of some of these diseases will be briefly discussed below. It should be recognized from the outset that it is extremely difficult to prove a causal relationship of a practice in early infancy with a disease that manifests itself only in adulthood and to which many factors may contribute. The problem is extemely important, however; the available evidence is in many cases suggestive, and the problem merits greater attention than it has thus far received.

83. Obesity. Although the health risks of obesity are well known, its etiology is not simple given its multiple origins . Once obesity has developed, treatment is difficult. Efforts should therefore be made for the better understanding of its etiology and natural history. One of the important questions that has not yet been answered concerns the relationship between feeding practices and overweight in infancy and childhood and obesity later in life. Although no long-term prospective studies are available, retrospective and short-term prospective studies tend to support the hypothesis of a relationship between obesity in infancy and its occurrence later in life.

84. Studies of the relationship between overweight at birth and obesity in childhood have in general showed a very low correlation.[45] A better correlation has been found between obesity at twelve months of age and later in life.[46] It has also been found that cases of severe obesity have a greater tendency to persist. One of the limitations of these studies is that they use as a basis for comparison situations at one point during infancy, for example at birth or at twelve months of age; there are, however, many non-dietary factors that may help to explain the situation at any given moment.

85. Weight gain during infancy has shown a better correlation with overweight later in life.[47] Available evidence seems therefore to suggest that overfeeding in infancy may be a factor contributing to later obesity. In this regard a recent prospective study showed that, while breast-fed and artificially fed infants had similar growth during the first three months of life, weight gain was greater for the artifically fed infants with a difference at one year of 410 g more in boys and 750 g in girls.[48] Overfeeding is, in fact, one of the risks of bottle-feeding and complementary feeding.

86. Breast-fed infants seem to regulate their intake in accordance with their needs. Once the mother takes over in deciding the amount of food the child should receive, overfeeding becomes a possibility. In many civilizations the image of a healthy baby is one that is overweight. Overconcern about infant nutrition can lead to overfeeding of the infant. The consequences later in life may be related to the infant's excess weight or to the acquisition of undesirable eating practices.

87. Hypertension. A high sodium intake is certainly one of the factors in the etiology of essential hypertension. A direct relationship is not easy to prove because there also seem to be contributing genetic factors, which make some individuals more sensitive than others to high salt intake. However, the relationship between high salt intake and hypertension has been proved experimentally in rats. What is most disturbing are the experimental data showing that sensitive rats having a high salt intake only during their first six weeks of life developed hypertension one year later even though they were returned, after the first six weeks, to a normal low-salt diet.[49]

88. Breast milk has a low sodium content (about 15 mg/100 ml or 6.5 mmol/1). The sodium intake of infants can increase drastically when complementary foods are introduced (see Table 1, part B). The situation is particularly serious when an infant's food is prepared to the taste of a mother whose salt intake is high. There are no data available concerning human beings to show, as has been demonstrated in experimental animals, that early high sodium intake has consequences later in life. It has been suggested, however, that the taste for salt may be established by the introduction of the first foods other than milk. The maintenance of this habit may then have a cumulative effect resulting in ill health many years later.

89. Experimental and epidemiological evidence indicates that potassium plays a protective role where high sodium intake in relation to hypertension is concerned.[50] While fresh vegetables and fruits have a high potassium content, their processing for use in complementary infant feeding may drastically reduce their value as sources of potassium as well as vitamin C.

90. An association has also been found between hypertension and obesity, although they may be etiologically unrelated and observed independantly. Early feeding practices may be a common factor that creates food habits favouring the development of both conditions.

91. Arteriosclerosis. There is no doubt about the role of dietary factors in the pathogenesis of arteriosclerosis and ischaemic heart disease, which is one of the major health problems of Western civilization. The dietary factors involved include high energy intake, and diets rich in cholesterol and saturated fats but low in polyunsaturated fats. High protein intake has also been found to be associated with these conditions. The role of the diet, however, is only contributory in individuals who are otherwise predisposed to them. The relationship of dietary factors to the development of the disease has been proved through epidemiological studies, prospective as well as cross-sectional comparisons between different populations.

92. It is very difficult to establish the relationship at the individual level, however, because people respond differently to a diet rich in saturated fats, and there are many other variables involved. It would be even more difficult to establish a relationship between infant dietary practices and a disease that will manifest itself only some 40 years later. It has been shown, however, that infants in the upper centiles of lipid blood levels tend to maintain those same levels two years later, a situation that has been called "tracking".[51] It makes sense, therefore, to avoid in complementary feeding the dietary excesses that have proved to be undesirable later in life.

93. Food allergy. There is evidence that prolonged breast-feeding and the not-too-early initiation of complementary feeding using carefully selected foods is of value in preventing the development of food allergies, particularly in predisposed infants.[52] The situation is very clear where cow's-milk allergy is concerned, but has also been shown to be so for other foods. Cow's-milk allergy is manifested by gastrointestinal, dermatological or respiratory symptoms of varying severity and even by anaphylactic shock, when the infant is exposed to unmodified or modified cow's milk.

94. It has been demonstrated by sensitive immunological methods that the majority of infants fed artificially with cow's-milk-based formulas do react to the foreign proteins. However, since only a few infants show clinical manifestations, and usually only those with severe symptomatology are diagnosed as having cow's-milk allergy, it is very difficult to know the real incidence of the disease. Various studies give an estimated prevalence of about 1% of clinical manifestations in industrialized countries where the majority of infants have received cow's-milk-based formulas since very early in life.[53] The condition can be prevented by avoiding the use of cow's-milk preparations, particularly during the neonatal period and the first few months of life.

95. It has been shown that prolonged breast-feeding also has a protective value with regard to allergies to other foods. In a study of infants born of parents suffering from eczema, it was demonstrated that a significant reduction in the incidence of the disease could be achieved by exclusive breast-feeding for at least three months and avoidance of allergenic foods during the initial stages of complementary feeding.[54] In another prospective study of children followed from birth up to three years of age, it was shown that infants who were breast-fed for six months had a lower incidence of atopic diseases, particularly those with a family history of allergies, than those who were artificially fed. Complementary feeding was started at three and a half months with cooked vegetables and fruits, cereals were introduced at five months, and meat and eggs were provided at six; a more varied diet was given by nine months of age.[52]

CONCLUSION

96. Lactation is a continuation, at the beginning of extrauterine life, of the fetal mechanism by which the child is fed by the mother with a food that is nutritionally complete and balanced. Very little physiological effort is thereby required by the digestive and excretory systems of the infant, which are not yet fully developed. Lactation also extends the period of protection against environmental aggressions until the infant is better prepared to cope with them.

97. Complementary feeding on the other hand is the beginning of an independant life. The diet required is a transition between lactation and the mixed and varied diet of the adult. Its introduction should not be delayed past the time when breast milk becomes insufficient as the only food for the infant; but to start it sooner than is necessary, in terms of the nutritional needs of the child, may be dangerous. Also, the infant may not be physiologically mature enough to handle complementary foods and the advantages of breast-feeding will be lost. The consequences may be immediate health risks, such as a greater susceptability to infectious diseases, particulary diarrhoea; or long-term ones, which are much more difficult to link directly with inappropriate infant feeding practices, but which are nevertheless significant, for example, a greater predisposition to allergies, obesity and arteriosclerosis.

98. No specific foods are required as a complement to lactation. They can vary with the availability and customs of the family, but should be nutritionally and physiologically adequate according to the needs and developmental stage of the infant. There is no precise age at which complementary feeding should be started; it should be determined by the stage of functional maturation of the infant and the ability of the mother's milk to satisfy the infant's nutritional requirements. For most normal infants this occurs between four and six months of age. Earlier complementary feeding may be required in exceptional cases; on the other hand, it may sometimes be more appropriate to start such feeding later than could be possible, in order to prolong the advantages of breast-feeding.

REFERENCES

1. HERBST, J.J., Development of sucking and swallowing. In: Lebenthal, E. (ed.) A textbook of gastroenterology and nutrition in infancy. Vol.1, New York, Raven Press., 1981, p. 102.

2. AURICCHIO, S. RUBINO, A. & MURSET, G. Intestinal glycosidase activities in the human embryo, fetus, and newborn. Pediatrics., 35:944 (1965).

3. LEBENTHAL, E. & LEE, P.C. Development of functional response in human exocrine pancreas. Pediatrics, 66:556 (1965).

4. LEBENTHAL, E. & LEE, P.C. Glucoamylase and disaccharidase activities in normal subjects and in patients with mucosal injury of the small intestine. J. Pediatr., 97:389 (1980).

5. LILIBRIDGE, C.B. & TOWNES, P.L. Physiologic deficiency of pancreatic amylase in infancy: A factor in iatrogenic diarrhea. J. Pediatr., 62::279 (1973).

6. LEBENTHAL, E. HATCH, T.F. & LEE, P.C. Development of disaccharidase in premature, small-for-gestational-age and full-term infants. In: Lebenthal, E. (ed.) A textbook of gastroenterology and nutrition in infancy. New York, Raven Press, 1980, p. 417.

7. AGUNOD, M. et al. Correlative study of hydrochloric acid, pepsin and intrinsic factor secretion in newborns and infants. Am. J. Dig. Dis., 14:400 (1969).

8. DEREN, J.S. Development of structure and function in fetal and newborn stomach. Am. J. Clin. Nutr., 24:144 (1971).

9. HADORN, B. Developmental aspects of intraluminal protein digestion. In: Lebenthal, E. (ed.) A textbook of gastroenterology and nutrition in infancy. New York, Raven Press, 1980, p. 368.

10. WALKER, W.A. et al. Intestinal uptake of macromolecules; effect of oral immunization. Science, 177:608 (1972).

11. ZOPPI, G. et al. Exocrine function in premature and full term neonates. Pediatr. Res., 6:880 (1972).

12. POLEY, J.R. et al. Bile acids in infants and children. J. Lab. Clin Med., 63:838 (1964).

13. HAMOSH, M. & BURNS, W.A. Lipolytic activity of human lingual glands (Ebner). Lav. Invest., 37:603 (1977).

14. HALL, B. & MULLER, D.P.R. Studies on the bile salt stimulated lipolytic activity of human milk using whole milk as source of both substrate and enzyme. I. Nutritional implications. Pediatr. Res., 16:251 (1982).

15. WEIJERS, A.A. et al. Analysis and interpretation of fat-absorption coefficient. Acta Pediatr., 49:615 (1982).

16. SAARINEN, U.M. SIIMES, M.A. & DALLMAN, P.R. Iron absorption in infants: High bioavailability of iron as indicated by the extrinsic tag method of iron absorption and by concentration of serum ferritin. J. Pediatr., 91:36 (1977).

17. OSKI, F.A. Development of the small intestine's capacity to absorb iron and folic acid. In: Lebenthal, E. (ed.) Textbook of gastroenterology and nutrition in infancy. New York, Raven Press. 1981, p. 612.

18. APERPIA, A. et al. Development of renal control of salt and fluid homeostasis during the first year of life. Acta Paediatr. Scand., 64:393 (1975).

19. SVENNINGSEN, N.W. & LINDQUIST, B. Postnatal development of renal hydrogen iron excretion in relation to age and protein intake. Acta Paediatr. Scand., 63:721 (1974).

20. OPPE, T.E. et al. Calcium and phosphorous levels in healthy newborn infants given various types of milk. Lancet, i:1045 (1968).

21. FOMON, S.J. & FILER, L.J. Amino acid requirements for normal growth. In: Nyhan, W.L., (ed.) Amino acid metabolism and genetic variation. New York, McGraw-Hill, 1967, p. 391.

22. WHO Technical Report Series No. 724, 1985, Geneva, Energy and requirements: report of a Joint FAO/WHO/UNU Expert Consultation. pp. 64-66.

23. FAO/WHO, WHO Technical Report Series No. 522, 1973, Geneva, Energy and protein requirements: report of a Joint FAO/WHO Ad Hoc Expert Committee.

24. FOMON, S.J. Infant nutrition, Philadelphia, Saunders; (1967).

25. FAO Nutritional Studies No. 15, 1957, Rome, Calorie requirements: report of the Second Committee on Calorie Requirements.

26. WATERLOW, J.C. & THOMSON, A.M. Observations on the adequacy of breast-feeding. Lancet, ii:238 (1979).

27. WHO Technical Report Series No. 724, op. cit., pp. 90-92.

28. WHITEHEAD, R.G. PAUL, A.A. & COLE, T.J. A critical analysis of measured food intakes during infancy and early childhood in comparison with current international recommendations. J. Human Nutr., 35:339 (1981).

29. HABICHT, J.P. et al. Height and weight standards for pre-school children. How relevant are ethnic differences in growth potential? Lancet, i:611 (1974).

30. AHN, C.H. & MACLEAN Jr. W.C. Growth of the exclusively breast-fed infant. Am. J. Clin. Nutr., 33:183 (1980).

31. WELSH, J.K. et al. Effect of antiviral lipids, heat, and freezing on the activity of viruses in human mil. J. Infect. Dis., 140:322-328 (1979).

32. HOLMGREN, J. SVENNERHOLM, A-M., & LINDBLAD, M. Receptor-like glycocompounds in human milk that inhibit classical and El Tor Vibrio cholerae cell adherence (hemagglutination). Infect. Immun., 39:147-154 (1983).

33. HANSON, L.A. & BRANDTZAEG, P. The mucosal defense system. In: Stichm, E. & Fulginitt, V.A. (eds.) Immunologic disorders in infants and children. Philadelphia, Saunders, 1979, pp. 137-164.

34. KLEINMAN, R.E. & WALKER, W.A. The enterommamary immune system: an important new concept in breast milk host defense. Dig. Dis. Sci., 24:876 (1979).

35. GLASS, R.I. et al. Protection against cholera in breast-fed children by antibodies in breast-milk. N. Engl. J. Med., 308:1389-1392 (1983).

36. GOLDMAN, A.S. et al. Immunologic factors in human milk during the first year of lactation. J. Pediatr., 100:563-567 (1982).

37. CRUZ, J.R. & AREVALD, C. Fluctuation of specific IgA antibodies in human milk. Acta Paediatr. Scand., 74:897-903 (1985).

38. GORDON, J.E. CHITKKARA, I.D. & WYON, J.B. Weanling diarrhea, Am. J. Med. Sci., 245:345-377. (1963).

39. BLACK, R.E. et al. Contamination of weaning foods and transmission of enterotoxigenic Escherichia coli diarrhoea in children in rural Bangladesh. Trans. R. Soc. Trop. Med. Hyg., 76:259-264 (1982).

40. VAN STEENBERGEN, W.M., et al. Machakos project studies. Agents affecting health of mother, infant and child in a rural area of Kenya. XXII. Bacterial contamination of foods commonly eaten by young children in Machakos, Kenya. Trop. Geogr. Med., 35:193-197 (1983).

41. SAMADI, A.Z., HUQ, M.I. AHMED, Q.S. Detection of rotavirus in hand-washing of attendants of children with diarrhoea. Br. Med. J., 286:188 (1983).

42. KHAN, M.V. Interruption of shigellosis by hand-washing. Trans. R. Soc. Trop. Med. Hyg., 76:164-168 (1982).

43. HERBERT, J.R. Effects of water quality and water quantity on nutritional status: Findings from a South Indian community. Bull. Wld. Hth. Org., 63:143-155 (1985).

44. JIWA. S. KROVACEK, K. & WADSTROM, T. Enterotoxigenic bacteria in food and water from an Ethiopian community. Appl. Environ. Microbiol., 41:1010-1019 (1981).

45. FISCH, R.O. et al. Obesity and leanness at birth and their relationship to body variations in later childhood. Pediatrics., 56:521 (1975).

46. JOHNSTON, F.E. & MARCK, R.W. Obesity in urban black adolescents of high and low relative weight at one year of age. Am. J. Dis. Child., 132:862 (1978).

47. EID, E.E. Follow-up study of physical growth of children who had excessive weight gain in first six months of life. Br. Med. J., 2:74 (1970).

48. HITCHCOCK, N.E. GRACY, M. & GILMOUR, A.I. The growth of breast-fed and artifically fed infants from birth to twelve months. Acta Paediatr. Scand., 74:240 (1985).

49. DAHL, L.K. HEINE, M. TAGSINARI, L. J. Exp. Med., 115:1173 (1962).

50. JAMES, W.P.T. Diseases of Western civilization. In: McLaren D.S., & Burman, D. (eds.) Textbook of paediatric nutrition. 2nd ed. Edinburgh, Churchill Livingstone, 1982, p. 419.

51. MELLIES, M. & GLUECK, Ch. Infant feeding practices and the development of atherosclerosis. In: Lebenthal, E. (ed.) Textbook of gastroenterology and nutrition in infancy, Vol. 2. New York, Raven Press, 1981 p. 722.

52. SAARINEN, U.M. et al. Prolongued breast-feeding as prophylaxis for atopic disease. Lancet, ii:163 (1979).

53. SAVILAHTI, E. KUITUNEN, P. VISAKORPI, J.K. Cow's milk allergy. In: Lebenthal, E. (ed.) Textbook of gastroenterology and nutrition in infancy. New York, Raven Press, 1981, p. 690.

54. MATTEW, D.J. et al. Prevention of eczema. Lancet, i:321 (1977).

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