PROCEEDINGS OF THE NUTRITION SOCIETY

The Three Hundred and Eighty-second Scientific Meeting (One Hundred and Forty-ninth Scottish Meeting) was held in the Craigie College of Education, Ayr, on 7/8 April 1983

SYMPOSIUM ON 'MILK COMPOSITION AND ITS MANIPULATION'

Milk composition—the infant human diet

By F. COCKBURN, *Department of Child Health, University of Glasgow, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ*

A mature human infant is able to suckle within minutes of birth and thus begin to safeguard his future. Having been protected within the uterus from a potentially hostile environment, after birth he must begin to adapt to this environment with maternal help. In the continuum of care and protection from conception until early childhood independence, suckling and lactation will play a key role in successful child rearing. The mother provides, or should continue to provide, the protection and nutrition required by her infant after birth.

Protection against infection

The mother will normally immediately colonize her infant with bacteria from her skin, mouth, nose and colostrum. Until birth the infant's skin, mucous membranes and intestinal tract are sterile yet within hours micro-organisms are established in these sites. Failure to establish a healthy symbiosis between the infant and microbes is not uncommon and deaths from infections still rank high in the causes of neonatal death and handicap.

Passive circulating immunity in the human infant is almost entirely from transplacentally acquired IgG and the pattern of protection within an individual infant will have been determined by the mother's immunological experience. Circulating maternal IgG falls to very low concentrations by 6 months of life and endogenous production within the infant, although possible before birth, does not achieve adult values until after the end of the first year of life. There is a trough in circulating infant IgG between 3 and 6 months of life. After birth, human colostrum provides 100 mg secretory IgA/ml which can give surface protection to mucous membranes and intestinal mucosa. Mature milk continues to provide approximately 4 mg/ml during the period of lactation (McClelland *et al.* 1978).

This secretory IgA contains specific immunoglobulin determined by the types of micro-organisms to which the mother had been exposed in her life (Allardyce *et al.* 1974; Goldblum *et al.* 1976; Ogra & Dayton, 1980). Achievement of ecological equilibrium between the infant and micro-organisms in the environment is essential to good health and is dependent upon not only the immunoglobulins provided by the mother, but also on the integrity of the infant skin and mucous membranes and by the virulence of the organisms to which he is exposed.

Colostrum contains, in addition to secretory IgA, large numbers of protective cells including polymorphonuclear leucocytes, macrophages and both T and B lymphocytes. Other protective materials identified in colostrum include complement, lysozyme, lactoferrin, lactoperoxidase and fatty acids, particularly linoleic, lauric and palmitoleic (Anon., 1981; Blanc, 1981; Goldman *et al.* 1982). Free fatty acids of sebaceous secretions protect skin and fatty acids in colostrum and milk inhibit the growth of some bacteria in the gut.

Despite the existence of these multiple mechanisms which control microbial populations at mucosal surfaces, the mucous membranes remain the most important portal of entry for microbial infections.

The bifidobacteria, which colonize the small intestines of breast-fed human infants (Tissier, 1899), are encouraged by the presence of a bifidus factor within human milk (Beerens *et al.* 1980) but perhaps more importantly this organism is transmitted directly from the ampullae of the nipple where it is normally resident. Antibiotic treatment of the mother will alter the nature of bacterial colonization within the ampullae and the bifidus organism is susceptible to most antibiotics (Rolles *et al.* 1982). During the first 72 h after birth, colonization of the mucous membranes, with or without bifidus, and skin with a wide variety of potentially pathogenic organisms is established. These organisms can originate from mother's milk. Cytomegalovirus, rubella, hepatitis B surface antigen, *Mycobacterium tuberculosis, Escherichia coli, Staphylococcus aureus* and streptococci have all been identified in fresh human milk (Hayes *et al.* 1972; Linneman & Goldberg, 1974; Buimovicci-Klein *et al.* 1977; Ogra & Dayton, 1980; Stagno *et al.* 1980). It is evident that human infants can survive microbial colonization without the benefit of colostrum and maternal organisms: not only do infants survive being given cow's and other modified milks which do not contain any protective cells or immunoglobulins by nurses harbouring micro-organisms completely foreign to the infant's natural environment, but they appear to thrive and grow normally. The series of interactions which safeguard infants in an unsophisticated society is so complex that it is difficult to understand, but when man introduces other confounding variables such as artificial sterile feeds, antibiotics and antiseptics any consideration of the quality of the infant's life and subsequent development is a value judgement difficult to subject to scientific analysis.

In times past in the UK (Robinson, 1951; Crosse, 1952), and at present in developing countries, infants who are breast-fed suffer less from infection affecting the gastrointestinal and respiratory tracts than artificially-fed infants (Cussen, 1980).

Nutrition

In any consideration of the nutritional adequacy of a particular milk, the ability of each infant to utilize milk effectively will depend on his genetic make-up and his maturity. The infant with phenylketonuria, due to an inherited defect in phenylalanine hydroxylase activity, could become severely mentally handicapped unless given a milk with a low phenylalanine and high tyrosine content. In this extreme example, mother's milk alone would not be the best nutritional substance for that infant. It is now nearly 20 years since an effective neonatal screening programme for phenylketonuria was introduced in some parts of the UK and the normal intelligence and growth of infants treated with a completely synthetic diet for the first months of life is testament to the nutritional adequacy of such diets during early growth and development. What is not yet known and what will be interesting to observe is whether individuals given such diets undergo degenerative processes more rapidly than infants who have been given human milk during infancy. I am unaware of any long-term controlled study in man of the beneficial and adverse effects of feeding the processed milk of the cow to infants during most of the first year of life. There has been much speculation, rumour and innuendo linking degenerative disorders, e.g. coronary artery disease, degenerative brain disorders, obesity and hypertension with 'artificial' feeding in infancy but little real evidence: some of the available evidence has been reviewed (Barltrop, 1977; Crawford & Sinclair, 1977; Ball & Brook, 1978).

Compositions of human milk and formulated milks

Table 1 gives a nutritional comparison of mature human milk, cow's milk and formulated milks available in the UK (Barr, 1982). Two sets of values are shown for mature human milk, the first obtained by the Department of Health and Social Security (1977, 1980*a*,*b*) from milk collected from a number of centres throughout the UK in 1976 and the second predominantly by Macy *et al.* (1953) from mothers in the USA prior to 1953. The differences shown in mineral, trace element and vitamin concentrations might be methodological or could be a reflection of true differences. Human milk composition in healthy, well-nourished women is known to vary; for example, fat content varies within a given feed, with the time of day and with the stage of lactation and some women consistently produce milk with a higher average fat content than others (Prentice *et al.* 1981*a*,*b*). Milk from malnourished and sick women has small but physiologically significant reductions in protein, carbohydrate and fat (Jelliffe & Jelliffe, 1978) and marked reductions in folate (Prentice, 1980), thiamin (Rajalakshmi, 1980), riboflavin (Bates, Prentice & Watkinson, 1982) and vitamin C (Bates, Prentice, Prentice *et al.* 1982).

Variations between the chemical compositions of human milk and formulated milk are consistently greater than variations between milk from different human mothers in terms of most individual carbohydrates, fatty acids, amino acids, minerals and vitamins.

Table 1. *Nutritional comparison of mature human milk, cow's milk and formulated milks available in the UK (Barr, 1982)*

(Composition per litre)

	Mature human milk										
Macronutrients	DHSS (1977, 1980*a*,*b*)	Macy *et al.* (1953)	Osterfeed baby milk*	Premium†¶	SMA goldcap‡¶	Ostermilk complete formula*¶	Ostermilk two*¶	Plus†¶	SMA‡¶	Milumil§¶	Cow's milk**
Protein (nitrogen × 6·38) (g)	13·4	14·5	14·5	15	15	17	18	19	15	18·5	34
Casein:whey value	—	32:68	39:61‖	33:67‖	40:60‖	77:23‖	77:23‖	77:23‖	82:18‖	80:20	77:23‖
Fat (g)	42	38	38·2	38	36	26	24	35	36	31	39
Saturated (%)	50·1	52	39·5	47·5	46·7	39·5	63·4	47·5	46·7	53·5	63·2
Unsaturated (%)	48·5	48	60·5	52·5	53·1	60·5	36·6	52·5	53·1	46·5	36·6
Carbohydrate (as disaccharide) (g)	70	70	70	72	72	86	83	69	72	84	46
Lactose (g)	70	70	70	72	72	28	53	69	72	60	46
Maltodextrin (g)	—	—	—	—	—	58	30	—	—	13	—
Amylose (g)	—	-	—	—	—	- -	—	—	—	11	—
Energy											
(kJ)	2930	2850	2840	2840	2750	2730	2600	2720	2750	2860	2800
(kcal)	700	680	680	680	650	650	620	650	650	680	670
Minerals											
Sodium (mg)	150	150	190	180	150	310	310	280	260	270	520
Potassium (mg)	600	550	570	600	560	700	790	890	740	860	1550
Chloride (mg)	430	430	440	570	400	560	580	570	470	440	980
Calcium (mg)	350	330	360	400	440	610	650	660	560	710	1240
Magnesium (mg)	28	40	52	45	53	60	64	60	53	70	120
Phosphorus (mg)	150	150	310	270	330	490	530	530	450	550	980

Trace elements											
Iron (mg)	0·76	1·5	6·5	6·5	6·7	6·5	6·5	6·5	6·7	7·0	0·5
Copper (μg)	390	400	430	—	500	390	160	—	500	130	200
Manganese (μg)	ND	7	12	100	160	33	10	100	160	110	ND
Zinc (mg)	2·95	5·3	3·5	3·4	3·7	3·3	2·0	3·4	3·7	2·24	3·6
Iodine (μg)	70	70	45	34	70	100	110	34	70	ND	ND
Renal solute load (mosm/l)	88	91	93	99	92	115	122	127	103	120	225
Vitamins											
A (μg)	600	530	1000	800	790	970	950	800	790	610	400
D (μg)	0·1	0·1	10	11	10·5	10	10	11	10·5	10	0·2
E (mg)	3·5	5·6	4·8	10	9·5	4·6	4·5	10	9·5	6	0·9
K (μg)	ND	17	27	28	58	26	15	28	58	40	ND
B_1 (μg)	160	160	420	700	800	390	380	700	800	400	400
B_2 (mg)	0·31	0·426	0·55	1·0	1·1	0·53	0·51	1·0	1·1	0·5	2·0
Niacin/niacinamide (mg)	2·3	1·72	6·9	8·5	10·0	6·5	6·4	8·5	10·0	4·0	0·8
B_6 (μg)	60	110	350	800	510	330	320	800	510	300	400
B_{12} (μg)	0·1	Trace	1·4	1·1	1·1	1·3	1·3	1·1	1·1	1·5	3·0
Folic acid (μg)	52	1·8	34	35	53	32	31	35	53	100	50
Pantothenic acid/ calcium pantothenate (mg)	2·6	1·96	2·3	2·5	2·1	2·2	2·2	2·5	2·1	4·0	3·6
Biotin (μg)	7·6	4·0	10	31	15	9·7	9·5	31	15	11	21
C (mg)	38	43	69	55	58	64	62	55	58	60	15

DHSS, Department of Health and Social Security.
ND, not determined.
*Farley Health Products Ltd (Glaxo Group Ltd), Plymouth, Devon.
†Cow & Gate Ltd, Trowbridge, Wiltshire.
‡John Wyeth, Maidenhead, Berkshire.
§Milupa Ltd, Hillingdon, Middlesex.
‖DHSS (1977, 1980*a*,*b*).
¶Manufacturer's information.
**Paul & Southgate (1978).

Requirements for milk

Infants' intakes of human and other milks vary considerably. At 2 months of age, solely breast-fed infants' intakes ranged from 445 to 1235 ml/d and these differences could not be accounted for in terms of the infants' body-weights and growth velocities (Whitehead & Paul, 1981). It is possible that some infants with a particular genetic endowment are relatively more efficient than others in their utilization of specific nutrients and can better survive famine conditions (Whitehead, 1983).

The chemical and physical composition of the diet influences the concentrations of nutrients entering the circulation and bathing the growing, developing and multiplying cells of the newborn tissues. Fig. 1 shows the different concentrations of plasma amino acids in three groups of thirty, term infants given three different proprietary formulae compared with those obtained from thirty, term infants given human milk during the first 6 months of life. There were significantly greater concentrations of plasma urea in all three groups of artificially-fed infants (Belton *et al.* 1977). Individual cells in the tissues of the infants in each of these groups must absorb, sift and process the available amino acids which are presented to them in a relatively random manner. Gross amino acid imbalance may block membrane transport and protein synthesis but smaller imbalances are tolerated.

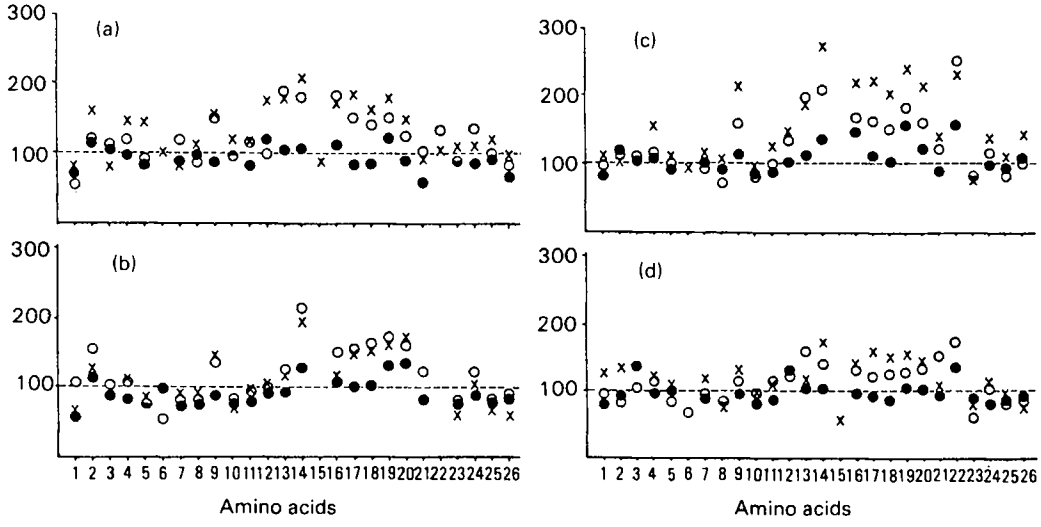

Fig. 1. Plasma amino acid concentrations measured in groups of thirty healthy infants born at term and of appropriate weight, having one of three cow's-milk based formulae (×, ○, ●) relative to values obtained in thirty infants given human milk (— — —). Capillary blood samples were taken at 11.00 hours at least 3 h after a feed from each of the 120 infants studied (Belton *et al.* 1977). Age of infants: (a), 3 weeks; (b), 3 months; (c), 6 weeks; (d), 6 months. Amino acids: 1, taurine; 2, aspartic acid; 3, hydroxyproline; 4, threonine; 5, serine; 6, asparagine; 7, glutamic acid; 8, glutamine; 9, proline; 10, glycine; 11, alanine; 12, citrulline; 13, α-aminobutyric acid; 14, valine; 15, cysteine; 16, methionine; 17, isoleucine; 18, leucine; 19, tyrosine; 20, phenylalanine; 21, tryptophan; 22, ethanolamine; 23, ornithine; 24, lysine; 25, histidine; 26, arginine.

https://doi.org/10.1079/PNS19830044 Published online by Cambridge University Press

Amino acids required for peptide and protein synthesis are retained and integrated, other amino acids return unchanged to the extracellular and plasma compartments and some are utilized for conversion to energy, producing urea as a waste product. This scavenging process may be better developed in some tissues than in others (Wheatley & Inglis, 1980). In the vulnerable human infant this could have important implications for normal brain growth, development and function. Glial cells have an important intermediary role in the scavenging process and transfer of nutrients to neurones.

Most estimates of breast-milk requirements have been based on the volumes necessary to satisfy energy requirements on the assumption that since breast milk is a perfectly balanced food all other nutrient requirements will be met. Previous estimates of energy requirements in term infants ranged from 0·5 MJ (120 kcal)/kg at 0–3 months of age to 0·46 MJ (110 kcal)/kg at 6 months (WHO/FAO, 1973) and were probably too generous. More recent analyses suggest that normal growth rates can be achieved in male infants with average daily intakes of 776 ml (0·44 MJ (104 kcal)/kg) at 2 months, 877 ml (0·39 MJ (91 kcal)/kg) at 4 months and 1005 ml (0·37 MJ (88 kcal)/kg) at 6–8 months. These results suggest that energy requirements per kg body-weight in UK infants are less and fall faster with age than had been previously supposed (Whitehead *et al.* 1981).

Control mechanisms regulating infant demand for milk and suckling vigour are probably extremely complex and involve *inter alia* smell, taste, gastrointestinal content and motility, gastrointestinal and other hormones (e.g. insulin, cholecystokinin, glucagon, bombesin and somatostatin) and the central appetite regulating systems mediated through amino acids, mono-amines and neuropeptides acting in the hypothalamus (Morley & Levine, 1983).

Low birth weight infants

Infants who grow poorly in utero ('light for date'; LFD) and preterm infants have in common a lack of nutritional reserve. Table 2 shows the relative body compositions of a 28-week preterm infant weighing 1 kg and a 40-week term infant of 3·5 kg. Of the total energy in the 1-kg infant, 2·02 MJ (480 kcal) are contained in protein and 0·46 MJ (110 kcal) in fat and carbohydrate. In the 3·5-kg term infant, the total nonprotein energy reserves are approximately 21 MJ (5000 kcal) or 6 MJ (1430 kcal)/kg. The fats and carbohydrates in the preterm and LFD infant are almost entirely structural and, in the absence of fresh nutrient supply, tissue breakdown must commence within hours and growth must cease. A term infant can utilize stores of fat and glycogen if there is delay in establishing feeding. There is very little reserve of free amino acids in infant tissues and tissue structural protein breakdown will occur to allow synthesis of new functional peptides and proteins such as hormones and enzymes after a few hours fasting.

After oxygen requirements have been met, the next immediate need for survival in the newborn infant is an adequate supply of water. It has been calculated that the 28-week gestation infant might survive for 3–4 d, the 40-week infant for 30 d

Table 2. *Body composition in preterm and term infants at birth*

Gestation (weeks) . . .	28	40
Body-weight (BW) (g)	1000	3500
Fat (g)	10	530
Fat-free BW (g)	990	2970
Extracellular water (g)	520	1400
Total water (g)	850	2400
Total water (g/kg fat-free BW)	859	808
Total water (g/kg total BW)	850	686
Carbohydrate (g)	5	34
Protein (g)	85	390
Minerals*		
Sodium (mmol)	94	286
Potassium (mmol)	42	185
Chloride (mmol)	68	192
Calcium (g)	6·3	33·6
Phosphorus (g)	3·9	19·6
Magnesium (g)	0·2	0·91
Iron (mg)	65	229
Copper (mg)	3·4	16·4
Zinc (mg)	20	70

*Expressed in terms of fat-free body tissue and adapted from results of Widdowson & Dickerson (1964).

and a well-nourished adult for 90 d if supplied with water alone. Growth cannot take place in these low birth weight infants until a minimum balanced fluid and nutrient intake supplying at least 0·46 MJ (110 kcal)/kg per d is achieved. In starvation a minimal catabolic energy release of 0·32 MJ (76 kcal)/kg per d is necessary to maintain life.

Differences between the preterm and LFD infants are related to organ maturity. In most situations the LFD infant tissues mature at a rate appropriate for the gestational age.

There may, however, be problems related to organ function engendered by the underlying cause of the intrauterine growth restriction. Thus an infant with growth restriction due to foetal alcohol syndrome has cellular deficits which will not allow that infant to achieve his genetic potential no matter how good post-natal nutrition might be. The functions of the preterm infant's liver, kidneys, skin, endocrine glands, gastrointestinal tract, exocrine glands and central nervous system limit the infant's ability to survive in the extra uterine environment.

The preterm infant

Feeding human milk or formulated milk to a preterm infant cannot be considered a physiological process (Cockburn, 1982*a*). There have been recent publications suggesting that milk from mothers who deliver a premature infant is better adapted to the immature infant's nutritional requirements in terms of energy and nitrogen intake (Atkinson *et al.* 1978; Gross *et al.* 1980; Gross, 1983). For the

very low birth weight infant (<1·3 kg), early maternal milk does not provide sufficient calcium and phosphorus (Atkinson *et al.* 1983). Mature, pooled, banked human milk provides insufficient protein and minerals to meet the nutritional requirements for the resumption of intrauterine rates of growth of infants born preterm (Gordon *et al.* 1947; Davies, 1977; Foman *et al.* 1977; Brady *et al.* 1982). Human milk, particularly preterm milk, is highly variable in composition and is often deficient in total energy, protein, sodium, calcium, phosphorus, copper, zinc and vitamins for the preterm infant's needs (Hibberd *et al.* 1982). However, when fresh maternal milk is available there are advantages including easy digestibility, probable protection against gut infections and necrotizing enterocolitis and maternal involvement with the infant at a time critical in the establishment of mother/infant love. The value of the mother's involvement and commitment in supplying milk for her preterm infant must not be underestimated.

The cellular content of preterm breast milk and its antibacterial activity is similar to that of mature breast milk (Murphy *et al.* 1983). Attempts have been made to adapt human milk by adding evaporated, expressed breast milk (EBM) to fresh EBM, but it seems unlikely that this will prove feasible for many preterm infants because of problems of supply and of costs (Lucas *et al.* 1980). Premature infant milk formulae containing a higher content of energy, whey and total protein, sodium, calcium, phosphorus and other minerals than mature infant milk formulae have been introduced. These do produce a faster weight gain in preterm infants than banked EBM and appear to be well-tolerated (Brook *et al.* 1982).

In most nurseries dealing with preterm infants, a combination of mother's fresh EBM, pooled banked EBM and premature formulae are given with a careful watch being kept for evidence of nutritional deficiencies manifest as oedema or vitamin E deficiency, radiological or biochemical evidence of rickets (which might be due to deficiencies of calcium, phosphorus, vitamin D or copper) and skin rashes due to vitamin or zinc deficiencies. Occasionally, in very low birth weight and sick preterm infants, parenteral nutrition may be required until enteral feeding can be tolerated. This combination of management reduces the time taken by low birth weight infants to regain birth weight and is associated with improved survival rates and with fewer survivors having significant handicaps (Cockburn, 1982*b*). There is certainly a need to continue the development of specialized milks for preterm infants.

Allergies

Adverse reactions to components in milks are dose dependent and the amount of the offending component absorbed depends on the dose and efficiency of the gut–mucosal barrier. Secretory IgA has an important role in defending the gut mucosa from penetration by foreign materials. There is also a genetic component, with some individual families being more susceptible to atopy. The mechanism for the hyporesponsiveness in non-atopic children does not appear to be due to the effectiveness of the mucosal barrier against milk proteins (e.g. β-lactoglobulin) but

may be related to systemic circulating IgA and the type of immune complex formed (Paganelli *et al.* 1983). The risk of developing an allergy to milk components is greatest in infancy and most infants develop antibodies of the IgG, IgA and IgM types (Peterson & Good, 1963). In atopic infants early antigenic exposure tends to cause a brisk increase in serum IgE values with subsequent sensitization of mast cells in the gastrointestinal and respiratory tracts and skin. Vomiting and diarrhoea, with failure to thrive, eczema, rhinitis and bronchitis are the major features of atopy in the young infant. Breast-feeding reduces the risk of developing atopic features in a genetically predisposed infant (Matthews *et al.* 1977; Saarinen *et al.* 1979).

Emotional aspects

There is more to breast-feeding than the provision of bacterial flora to line the gut, antimicrobial factors to safeguard against infections and nutrients to ensure growth. The whole mechanism of feeding in relation to maternal endocrine responses, in which oxytocin is released in response to the infant's hunger cry and prolactin is released in response to suckling, brings about a completely different relationship between bottle-fed and breast-fed infants and their mothers. In relation to the let-down reflex, sucking, swallowing and diurnal feeding pattern differences and interactions can be measured (Crow *et al.* 1980; McNeilly *et al.* 1983). The pattern of sucking and swallowing and the types of contact and interaction between mother and child are so different between bottle- and breast-fed infants that it is worth considering whether these significantly affect subsequent feeding and behaviour patterns (Wright & Crow, 1982). Dangers of underfeeding and overfeeding related to maternal anxieties and expectations and to infant demands and mother's interpretation of these demands are seen in everyday paediatric practice. Inadequate bonding is related to a higher incidence of non-accidental injury, particularly in preterm infants, and inadequate emotional provision is as damaging as inadequate nutritional provision to the young human infant.

Conclusion

A mature human infant obtains from mother's milk within a few days of birth sufficient balanced nutrients to grow at a rate determined by his genetic potential and the quantity and quality of the mother's milk. Rarely, the intake of unmodified human milk can be harmful as in infants with inherited metabolic defects such as galactosaemia and phenylketonuria. That human infants grow and develop when given a wide variety of modified and synthetic diets has been demonstrated not only in children requiring specialized diets for inherited metabolic defects, but in a majority of infants born in the UK between 1953 and 1973, who were given modified cow's milk formulae. This experiment was and still is uncontrolled and we have very little knowledge of any advantages or disadvantages accruing to the human infant and human adult from changing the whole nursing procedure

(bottles, teats, burping, etc.) and from feeding milk of one mammalian species to another.

There is a series of protective mechanisms in human milk which help to protect the infant from infections of the gastrointestinal and respiratory systems. Large numbers of protective cells including polymorphonuclear leucocytes, macrophages and T and B lymphocytes are present in human colostrum and milk, together with immunoglobulins (especially secretory IgA), complement, lysozyme, lactoferrin, lactoperoxidase, fatty acids (linoleic, lauric and palmitoleic) and specific factors such as the bifidus and the bifidus organisms. These and other, as yet unidentified, factors protect the infant against a wide range of microbes.

As a natural source of nutrients, human milk differs from milks of other mammals and a considerable ingenuity has been exercised in 'humanizing' cow's milk. Our knowledge of the average dietary requirements of infants is based on 'averaged' intakes of human milk at different ages. As intakes in different infants of the same maturity and body-weight can vary by as much as 100% and the chemical composition of human milks is subject to considerable variation and the apparent efficiency of utilization and bioavailability of vitamins and minerals varies, it is not surprising that nutritional guidelines for proprietary milk formulae are subject to frequent revision.

REFERENCES

Allardyce, R. A., Shearman, D. J. C., McClelland, D. B. L., Marwick, K., Simpson, A. J. & Laidlaw, R. B. (1974). *Br. med. J.* **3**, 307.

Anon. (1981). *Lancet* **i**, 1192.

Atkinson, S. A., Bryan, M. H. & Anderson, G. H. (1978). *J. Pediat.* **93**, 67.

Atkinson, S. A., Radde, I. C. & Anderson, G. H. (1983). *J. Pediat.* **102**, 99.

Ball, K. P. & Brook, C. G. D. (1978). *Postgrad. med. J.* **54**, 137.

Barltrop, D. (1977). *Paediatric Implications for Some Adult Disorders.* Unigate Paediatric Workshop. London: The Fellowship of Postgraduate Medicine.

Barr, R. I. (1982). *Nutritional Comparison of Infant Formulae Available in the United Kingdom.* Plymouth: Farley Health Products.

Bates, C. J., Prentice, A. & Watkinson, M. (1982). *Am. J. clin. Nutr.* **35**, 701.

Bates, C. J., Prentice, A. M., Prentice, A., Paul, A. A. & Whitehead, R. G. (1982). *Trans. Roy. Soc. Trop. Med. Hyg.* **76**, 341.

Beerens, H., Romond, C. & Neut, C. (1980). *Am. J. clin. Nutr.* **33**, 2434.

Belton, N. R., Cockburn, F. & Forfar, J. O. (1977). *Archs Dis. Childh.* **52**, 167.

Blanc, B. (1981). *World Rev. Nutr. Diet.* **36**, 1.

Brady, M. S., Rickard, K. A., Ernst, J. A., Schreiner, R. L. & Lemons, J. A. (1982). *J. Am. Diet. Assoc.* **81**, 547.

Brook, O. G., Wood, C. & Barley, J. (1982). *Archs Dis. Childh.* **57**, 898.

Buimovicci-Klein, E., Hite, R. L. & Byrne, T. (1977). *J. Pediat.* **91**, 939.

Cockburn, F. (1982*a*). In *Topics in Perinatal Medicine*, vol. 2, p. 66 [B. Wharton, editor]. London: Pitman.

Cockburn, F. (1982*b*). In *Metabolic Care*, p. 216 [D. E. F. Tweedle, editor]. Edinburgh: Churchill Livingstone.

Crawford, M. A. & Sinclair, A. J. (1977). In *Lipids, Malnutrition and the Developing Brain*, p. 267. CIBA Foundation Symposium. Amsterdam: Elsevier Excerpta Medica.

Crosse, V. M. (1952). *The Premature Baby.* London: Churchill Ltd.

Crow, R. A., Fawcett, J. N. & Wright, P. (1980). *J. behav. Med.* **3**, 259.

Cussen, G. H. (1980). In *Topics in Perinatal Medicine*, vol. 1, p. 79 [B. Wharton, editor]. London: Pitman.
Davies, D. P. (1977). *Archs Dis. Childh.* **52**, 296.
Department of Health and Social Security (1977). *The Composition of Mature Human Milk.* Report on Health and Social Subjects no. 12. London: H.M. Stationery Office.
Department of Health and Social Security (1980*a*). *Artificial Feeds for the Young Infant.* Report on Health and Social Subjects no. 18. London: H.M. Stationery Office.
Department of Health and Social Security (1980*b*). *Present Day Practice in Infant Feeding.* Report on Health and Social Subjects no. 20. London: H.M. Stationery Office.
Foman, S. J., Ziegler, E. E. & Vasquez, H. D. (1977). *Am. J. Dis. Childh.* **131**, 463.
Goldblum, R. M., Attlstedt, S. & Carlsson, B. (1976). *Nature* **257**, 797.
Goldman, A. S., Garza, C., Nichols, B. L. & Goldblum, R. M. (1982). *J. Pediat.* **4**, 563.
Gordon, H. H., Levine, S. Z. & McNamara, H. (1947). *Am. J. Dis. Childh.* **73**, 442.
Gross, S. J. (1983). *New Engl. J. Med.* **308**, 237.
Gross, S. J., David, R. J., Bauman, L. & Tomarelli, R. M. (1980). *J. Pediat.* **96**, 641.
Hayes, K., Danks, D. M. & Gibas, H. (1972). *New Engl. J. Med.* **287**, 177.
Hibberd, C., Brook, O. G., Carter, M. D., Haug, M. & Harzer, G. (1982). *Archs Dis. Childh.* **57**, 658.
Jelliffe, D. B. & Jelliffe, E. F. P. (1978). *Am. J. clin. Nutr.* **31**, 492.
Linneman, C. C. & Goldberg, S. (1974). *Lancet* **ii**, 155.
Lucas, A., Lucas, P. J., Chavin, S. I., Lyter, R. L. J. & Baum, J. D. (1980). *Early Hum. Develop.* **4**, 15.
McClelland, D. B. L., McGrath, J. & Samson, R. R. (1978). *Acta Paediat.* **271**, (Suppl.), 1.
McNeilly, A. S., Robinson, I. C. A. F., Houston, M. J. & Howie, P. W. (1983). *Br. med. J.* **286**, 257.
Macy, I. G., Kelly, H. J. & Sloan, R. E. (1953). *The Composition of Milks.* National Research Council Publication no. 254. Washington DC: National Academy of Sciences.
Matthews, D. J., Norman, A. P., Taylor, B., Turner, M. W. & Soothill, J. F. (1977). *Lancet* **i**, 321.
Mettler, A. E. (1976). *Postgrad. Med. J.* **52**, (Suppl.), 8.
Morley, J. E. & Levine, A. S. (1983). *Lancet* **i**, 398.
Murphy, J. F., Neale, M. L. & Matthews, N. (1983). *Archs Dis. Childh.* **58**, 198.
Ogra, P. L. & Dayton, D. H. [editors]. (1980). *Immunology of Breast Milk.* New York: Raven Press.
Paganelli, R. P., Atherton, D. J. & Levinsky, R. L. (1983). *Archs Dis. Childh.* **58**, 201.
Paul, A. A. & Southgate, D. A. T. (1978). *McCance and Widdowson's The Composition of Foods.* London: H.M. Stationery Office.
Peterson, R. D. A. & Good, R. A. (1963). *Pediatrics* **31**, 209.
Prentice, A., Prentice, A. M. & Whitehead, R. G. (1981*a*). *Br. J. Nutr.* **45**, 483.
Prentice, A., Prentice, A. M. & Whitehead, R. G. (1981*b*). *Br. J. Nutr.* **45**, 495.
Prentice, A. M. (1980). In *Maternal Nutrition During Pregnancy and Lactation*, p. 167 [R. G. Whitehead and H. Aebi, editors]. Berne: Hans Huber.
Rajalakshmi, R. (1980). In *Maternal Nutrition During Pregnancy and Lactation*, p. 184 [R. G. Whitehead and H. Aebi, editors]. Berne: Hans Huber.
Robinson, M. (1951). *Lancet* **i**, 788.
Rolles, C. J., Hall, M. A., Duncan, H. & Sampeys, C. (1982). In *Topics in Perinatal Medicine*, vol. 2, p. 31 [B. Wharton, editor]. London: Pitman.
Saarinen, U. M., Kajossaari, M., Backman, A. & Siimes, M. A. (1979). *Lancet* **ii**, 163.
Stagno, S., Reynolds, D. W. & Pass, R. F. (1980). *New Engl. J. Med.* **302**, 1073.
Tissier, M. H. (1899). *C.R. Acad. Sci.* **51**, 943.
Wheatley, D. N. & Inglis, M. S. (1980). *J. theoret. Biol.* **83**, 437.
Whitehead, R. G. (1983). *Lancet* **i**, 167.
Whitehead, R. G. & Paul, A. A. (1981). *Lancet* **ii**, 161.
Whitehead, R. G., Paul, A. A. & Cole, T. J. (1981). *J. Hum. Nutr.* **35**, 339.
WHO/FAO (1973). Energy and protein requirements. WHO *Techn. Rep. Ser.* no. 522, FAO *Nutr. Meetings Rep. Ser.* no. 52. Geneva/Rome: World Health Organization/Food and Agriculture Organization.

Widdowson, E. M. & Dickerson, J. W. T. (1964). In *Mineral Metabolism,* p. 11A [C. L. Comar and F. Bronner, editors]. New York: Academic Press.
Wright, P. & Crow, R. A. (1982). In *Psychobiology of the Human Newborn,* p. 339 [P. Stratton, editor]. London: John Wiley & Sons.

Printed in Great Britain