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Selenium concentration in milks

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In this review article, papers on selenium concentrations in cow and human milk are reviewed in order to identify the main factors that affect these concentrations as well as the Se intake of lactating infants. Selenium intake and Se status of the mother seem to be the main factors that influence Se concentrations in human milk. The progression of lactation can diminish the Se concentrations in human milk. Most authors have reported Se levels in human milk greater than Se levels in available milk formulas for infants from the same country. Thus, higher Se intakes in the breast-fed infant than Se intakes in formula-fed infants have been observed. Also, the Se compounds in breast milk seem to be more biologically available for infant nutrition than those in formulas.

NOTATION

GSH-Px	Glutathione peroxidase
INAA	Instrumental neutron activation analysis
RNAA	Radiochemical neutron activation analysis
EAAS	Electrothermal atomic absorption spectrometry
HG-AAS	Hydride-generation atomic absorption spectrometry
SPF	Spectrofluorimetry
CG	Gas chromatography
HPLC	High performance liquid chromatography

INTRODUCTION

Interest in the role of Se in human nutrition is increasing, as more and more investigators realise the essential nature of this trace element to human health (Levander, 1987). Although interest in Se was initially caused by its potential toxicity (Wilber, 1980), more important is its deficiency in several geographical areas. Low Se intakes have been associated with Keshan and Kashin-Beck diseases, juvenile cardiomyopathies that occur in certain parts of China (Keshan Disease Research Group, 1979; Levander, 1987; Khan, 1989). There are many other diseases that have been related to Se deficiency. Epidemiological studies have shown a relationship between low Se intake and increased risk of cancer (Clark, 1985; Combs & Clark, 1985; Yu *et al.*, 1985; Levander, 1987) or ischemic heart disease (Virtamo *et al.*, 1985; Levander, 1987; Bukkens *et al.*, 1990; Oster & Prellwitz, 1990).

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The main source of Se intake are foods. Milk of all animal species is notoriously low in trace elements (Picciano, 1985). Selenium concentration in milk is lower than the concentration of other essential trace elements (Cu or Zn) (Hatano *et al.*, 1985). Breast milk may be the main source of Se for breast-fed infants. Therefore, the section of the population most vulnerable to Se deficiency includes infants receiving breast or formula milk containing very low levels of Se and patients on restricted long-term diets (Lane *et al.*, 1981; Sando, 1989). Selenium requirements of children have been extrapolated from adult values on the basis of body weight, and an arbitrary factor allowed for growth. Thus, the Food and Nutrition Board (US) has proposed a lowest level of safe and adequate intake of Se for infants: 10 and 15 μg/day for infants of 0–0·5 years and 0·5–1 years, respectively (Committee on Dietary Allowances, 1989).

In this paper, we review the main data published from 1975 to 1992 on Se concentrations in human milk and commercial milk adapted for human consumption. Also, Se intakes for lactating infants from different geographical areas have been included. Given their relevance we have included some data from earlier years.

ANALYTICAL CONSIDERATIONS

Sampling and storage

Milk samples must be collected via a mechanical pump according to the standard procedures described in the IAEA/WHO document (Parr, 1978). All sample collection equipment was plastic or, more specifically,

polypropylene (Litov *et al.*, 1989), acid-washed to prevent Se contamination. Care should be taken when sampling mature human milk for estimation of Se concentration (Smith *et al.*, 1982) because, although these authors did not find differences in Se content throughout the day, samples should be collected from different feeds during the same day. Also, when possible, various samples were collected during the same feed (Vuori & Kuitunen, 1979; Clemente *et al.*, 1982).

Milk or colostrum samples were freeze-dried (Binnerts, 1979; Varo & Koivistoinen, 1981; Polkowska-Motrenko *et al.*, 1982) or frozen (Maus *et al.*, 1980; Debski *et al.*, 1987; Levander *et al.*, 1987; Mannan & Picciano, 1987) in liquid nitrogen (Smith *et al.*, 1982) or in solid carbon dioxide (Shearer & Hadjimarkos, 1975) immediately after sampling. Then the samples were stored at −14°C (Litov *et al.*, 1989), at −18°C (Karlsen *et al.*, 1981; Kumpulainen *et al.*, 1983*b*; Varo *et al.*, 1984), at −20°C (Smith *et al.*, 1982), at −70°C (Debski *et al.*, 1987; Mannan & Picciano, 1987), or kept in an ice bath (Smith & Picciano, 1986). Preservation of mature milk at −20°C decreased its GSH-Px activity linearly with time at a rate of 5·8 unit/ml/day (Hojo, 1986*a*). After thawing, the human milk samples were heated to 40°C and carefully mixed before analysis (Kumpulainen *et al.*, 1983*b*). Also human and cow's milk and formula samples were dried in silica tubes for 24 h at 70°C and thereafter for 8 h at 100°C (Lombeck *et al.*, 1978).

Sample treatment

For studying the distinct fractions of milk, diverse methods of fractionation have been applied. Skimmed milk has been prepared by centrifugation for 1·5 h at 4°C at 10 000 *g* (Debski *et al.*, 1987) or for 30 min at 2000 *g* (Avissar *et al.*, 1991) or at 1500 *g* (Yoshida *et al.*, 1981; Van Dael & Deelstra, 1989). After being centrifuged for 1 h at 120 000 *g* (4°C), the supernatant (whey) and pellet (mostly casein) fractions are obtained. After this, the samples have been dialyzed in membrane tubing with a molecular mass cutoff of 6–8 kDa for four days against deionized water (Debski *et al.*, 1987). Also, the pH of the skimmed milk adjusted to 4·6 to precipitate caseins (Van Dael & Deelstra, 1989). $CaCl_2$ and rennin have been employed in order to precipitate casein at 37°C for 5 h. Afterwards the whey fraction was separated from the casein coagulum by centrifugation at 1000 *g* for 15 min. Trichloroacetic acid (TCA) was added to the whey fraction and the suspension was subsequently centrifuged to separate it into TCA-soluble and TCA-insoluble fractions. On the other hand, the precipitated casein was washed with NaOH solution, subsequently collected by centrifugation, and dried in a vacuum (Yoshida *et al.*, 1981).

In the case of X-ray fluorescence, neutron activation analysis, and atomic absorption spectrometry with a graphite furnace, sample preparation can be kept to a minimum. So, the treatment of the sample was usually drying (Lombeck *et al.*, 1978) as no differences could be detected between the drying and ashing methods (Behne & Matamba, 1975). However, most techniques have used digestion as a sample treatment. Seleno-organocompounds in milk can resist oxidation except with $HClO_4$ mixture (Olson *et al.*, 1975; Nève *et al.*, 1982). However, other authors (Olson *et al.*, 1975; Bunker & Delves, 1987; Charlot *et al.*, 1989) do not find differences in the results when mixtures of HNO_3 and H_2SO_4 or HNO_3, H_2SO_4 and $HClO_4$ are added. Other digestion procedures have been proposed, such as the addition of HNO_3, H_3PO_4 and H_2O_2 in order to eliminate the need for a $HClO_4$ mixture (Reamer & Veillon, 1983; Macpherson *et al.*, 1988). Recently, a somewhat revolutionary method was developed for the digestion of organic and inorganic matrices in biological fluids which involves the use of microwaves (Cornelis, 1991; Feinberg, 1991; LamLeung *et al.*, 1991; Matusiewicz *et al.*, 1991).

Instrumental determination

There are many available methods to determine Se. Four important methods may stand out for the analysis of Se in milk: Instrumental Neutron Activation Analysis (INAA), Spectrofluorimetry (SPF), Gas Chromatography (GC), and Atomic Absorption Spectrometry (AAS).

Spectrofluorimetric methods are well established. They are based on the measurement of the sensitive fluorescence of piazselenols derived from selenite. Thus, the digested samples must be treated with HCl, heating to reduce the selenate to selenite (Lalonde *et al.*, 1982; Koh & Benson, 1983; Pettersson & Olin, 1991). Other reducing agents such as H_2O_2 (Michie *et al.*, 1978) or hydroxylamine (Holynska & Lipinska-Kalita, 1977; Peters & Koehler, 1982) have been used. The optimum pH and temperature/time for the formation of a fluorescent piazselenol with DAN (2,3-diaminonaphthalene) was studied by several authors (Lalonde *et al.*, 1982; Alfthan, 1984; Pettersson *et al.*, 1988). In order to eliminate interferences, this complex was extracted with a hydrophobic solvent such as cyclohexane, toluene, benzene, chloroform, etc. Afterwards, the fluorescence (λ_{ex} = 360 nm, λ_{em} = 520 nm) was measured in a fluorescence spectrometer (Watkinson, 1966). In biological materials and for concentrations of Se < 0·3 mg/kg fluorimetry has been selected as a reference method, because of its high precision, low detection limit, and complete recovery (Table 1).

New HPLC methods coupled to fluorescence detection of the piazselenol complex are being developed. These methods can be applied to human milk or paediatric samples where small quantities may be available and subnanogram sensitivity is required (Vézina & Bleau, 1988; Handelman *et al.*, 1989). Also, these chromatographic methods show promise because of the fact that the different Se species present in milk could be separated and determined, which would be interesting for bioavailability studies.

INAA, if available, can be valuable as a reference for validating alternative analytical methods. In general,

sensitivity and precision of INAA are lower than fluorimetric methods (Table 1), and both are capable of producing unbiased results (Heydorn & Griepink, 1990). However, INAA has several advantages with respect to fluorimetric methods. Thus, it is non-destructive and the only losses of concern are by escape of volatile compounds. The sample treatment can be reduced to a minimum. Exposure of the sample in a nuclear reactor for a few days yields only one long-lived isotope of Se, ^{75}Se. When the short-lived activation product ^{77m}Se was measured the time of analysis decreased significantly from three months to two days (Egan *et al.*, 1977; Woittiez & Nieuwendijk, 1987). Also, this method can be combined with radiochemical separation with orthodiamines in order to eliminate interference (Kalouskova *et al.*, 1989), but the RSD can increase (Sarudi *et al.*, 1989).

Selenium determination in biological fluids in the subnanogram range by AAS can be performed using the graphite furnace (EAAS) and the hydride-generation techniques (HG-AAS) (McCarthy *et al.*, 1981; Ringstad & Thelle, 1986). The two techniques (HG-AAS and EAAS) have been correlated satisfactorily (Oster & Prellwitz, 1982; Macpherson *et al.*, 1988). The best absolute detection limit can be observed in EAAS but HG-AAS is faster and cheaper (Verlinden *et al.*, 1981). An automated microtechnique for Se analysis, flow injection HG-AAS, is capable of performing a rapid and accurate Se determination at picogram levels in acid-digested biological fluids (Negretti de Brätter *et al.*, 1990). The relatively poor precision, losses, and interference are the main problems of both methods. Some authors (Koh & Benson, 1983) have left out the previous digestion step in the EAAS technique. But most authors (Neve *et al.*, 1980; Tôei & Shimoishi, 1981; Koops *et al.*, 1989) prefer to digest the samples of milk, and after carrying out an extraction process in order to eliminate interference. In order to stabilize or reduce the volatility of inorganic Se compounds of digested samples for direct determinations by EAAS, the addition of various metallic salts has been proposed. Salts of nickel are commonly used (Alexander *et al.*, 1980; Carnrick *et al.*, 1983). Also, a Mg–Pd system or Pd alone has a substantial equalizing effect on the atomization temperature (Schlemmer & Welz, 1986; Charlot *et al.*, 1989; Koops *et al.*, 1989). The use of Zeeman-effect background correction is widely recommended in biological matrices where iron and phosphorus are also present (Koops *et al.*, 1989; McMaster *et al.*, 1990; Hoenig, 1991; Welz *et al.*, 1983). In the HG-AAS technique, it is necessary to reduce, with borohydride, the selenate to selenite in the digested samples. Interferring ions in this step can be masked by addition of 1,10-phenanthroline, quinidine-8-ol or thiourea (Long & Yu, 1986).

Methodology available for the quantification of Se by GC was reviewed (Dilli & Sutikno, 1984*b*). In GC methods, digestion and reduction steps are necessary to determine Se in milk, as in fluorimetric methods. Afterwards the digested and reduced sample is treated with halogenated aromatic *o*-diamines to form piazselenols (Uchida *et al.*, 1981; Dilli & Sutikno, 1984*a*). The selenium complex is extracted in organic solvent and measured by the sensitive GC method with an electron capture detector (Cappon & Smith, 1978; Uchida *et al.*, 1981). However, the sensitivity of GC is not as good as in the latter methods, although the reported precision is lower than those. Also, some authors (Cappon & Smith, 1978) have observed incomplete recovery (Table 1).

SELENIUM IN MILK

Occurrence

The total Se content does not give information on the overall utilization or bioavailability of the element. Selenium in human milk and other animal milks was positively correlated with its protein content (Millar & Sheppard, 1972; Smith *et al.*, 1982; Hojo, 1986*b*) and negatively correlated with its fat content (Hojo, 1986*b*). At least 8–12 selenoproteins could be identified after gel chromatography of dialyzed human milk (Debski *et al.*, 1987). Skimmed milk contained 93% of the total Se, which is mainly protein-bound; k-casein was the protein richest in Se, followed by β-casein (Van Dael *et al.*, 1991). Yoshida *et al.* (1981) have shown a major proportion of Se in the casein fraction of pasteurized bovine milk. The Se in the whey fraction is mainly in the free selenite form. Other investigators (Van Dael & Deelstra, 1989) have found especially, that β-lactoglobulin is a Se-rich protein, contributing up to 80% of the total Se content of the bovine whey. Separation treatment influences the Se content in each fraction obtained. So, only 1–3% of total milk Se remained in the lipid fraction after centrifugation. Approximately 20–28% of Se in milk was removed by dialysis but the loss of Se from dialysis was not uniform among fractions; there was a loss of 66% of the Se associated with the 10 kDa fraction in human milk. After ultracentrifugation, the supernatant fractions contained 62, 71, and 29% of the total milk Se collected from women, cows, and goats, respectively (Debski *et al.*, 1987). Consequently, the pellet obtained from goat's milk contained 65% more Se than the pellet from human milk and 204% more than that from cow's milk (Debski *et al.*, 1987).

The strong positive relationship ($r = 0{\cdot}81$, $p < 0{\cdot}001$) observed between Se concentration and GSH-Px activity of human milk suggests that a large portion of the Se in human milk is present as a part of this enzyme (Mannan & Picciano, 1987). This was verified by molecular sieve chromatography of human milk with GSH-Px and accounted for 15–30% of the Se in milk (Milner *et al.*, 1987). In cow's milk about 12% of Se was bound to GSH-Px (Hojo, 1982). Most of the GSH-Px activity was found in the fractions corresponding to 170 kDa and 96 kDa in milk from women, goat, and cow species examined (Milner *et al.*, 1987). There are two distinct forms of Se-dependent gluta-

Table 1. Literature data on determination of Se in milks

Method	Sample treatment	Detection limit (ng/ml)	RSD % between-assay (within-assay)	Recovery %	Ref.
SPF	$HNO_3/HClO_4$ digestion; HCl reduction; DAN; cyclohexane extraction	0·2 ng			Grant (1981)
SPF	$HNO_3/HClO_4$ digestion; HCl reduction; EDTA, DAN, cyclohexane extraction		10 (2)	100 ± 2·2 (97–100)	Koh & Benson (1983)
SPF	$HNO_3/HClO_4$ digestion; HCl reduction; EDTA, DAN, cyclohexane extraction		5		Koops *et al.* (1989)
EAAS	$HNO_3/HClO_4/H_2SO_4/H_2O_2$ digestion; NH_2OH reduction; 4-chloro-1,2-diaminobenzene; toluene extraction; $Ni(NO_3)_2$ modifier	50	4·0	102–107	Nêve *et al.* (1980)
EAAS with D_2 lamp	$HNO_3/HClO_4/H_2SO_4/H_2O_2$ digestion; HCl reduction; EDTA, Cu^{2+} complexation; APDC-MIBK extraction	0·6	7·3	98·4	Kumputainen *et al.* (1983*a*)
	$HNO_3/HClO_4/H_2SO_4/H_2O_2$ digestion; HCl reduction; Cu^{2+}; APDC-MIBK extraction			93·1	
	$HNO_3/HClO_4/H_2SO_4/H_2O_2$ digestion; HCl reduction; EDTA, Ni^{2+} complexation; APDC-MIBK extraction			82·1	
	$HNO_3/HClO_4/H_2SO_4/H_2O_2$ digestion; HCl reduction; EDTA, Cu^{2+} complexation; NaDDC-MIBK extraction			95·1	
EAAS with D_2 lamp	$HNO_3/HClO_4/H_2SO_4$ digestion; HCl reduction; EDTA, APDC-MIBK extraction; Cu^{2+} modifier		12·1		Varo *et al.* (1984)
EAAS	$HNO_3/HClO_4$ digestion; HCl reduction; DAN, cyclohexane extraction organic Ag-sulfonate/hydrocarbon oil	0·5	2		Norheim *et al.* (1983)
EAAS with D_2 lamp	HNO_3/H_2SO_4 digestion, urea; Triton X-100; $PdCl_2$ as matrix modifier		20		Charlot *et al.* (1989)
EAAS, Zeeman	Triton X-100 dilution; $Pd/Mg(NO_3)_2$ as matrix modifier		18		Koops *et al.* (1989)
HG-AAS	Oxygen combustion/silicic acid; dissolution in acid medium; $NaBH_4$	2 ng	1·6		Han *et al.* (1981)
HG-AAS with FIA	$HNO_3/HClO_4/H_2SO_4$ digestion; HCl reduction; $NaBH_4$	0·31	8–11		Negretti de Brätter *et al.* (1990)

INAA, Se^{75}	Dried at 70°C, 24 h and at 100°C, 8 h; $5 \cdot 10^{13}$ n/cm^2 · s, 48 h irradiation; 60–90 days of decay time		10		Lombeck *et al.* (1977); Lombeck *et al.* (1980)
INAA, Se^{75}	$2{\cdot}6 \cdot 10^{12}$ n/cm^2 · s, 10–14 h irradiation	1 ng/g	6·7		Clemente *et al.* (1982)
INAA, Se^{75}, Se^{77m}	Lyophilization; $5 \cdot 10^{13}$ n/cm^2 · s, 2 s irradiation; 5 s decay time; 10 s counting time	2 ng	15		Woittiez & Nieuwendijk (1987)
RNAA, Se^{75}	Lyophilization; oxygen flask combustion; HCl/H_2SO_4 digestion; DDTC/toluene extraction; $2 \cdot 10^{12}$ n/cm^2 · s, 20–40 h irradiation				Polkowska-Motrenko *et al.* (1982)
RNAA, Se^{75}	Dried at 65°C; ethyl-α-isonitroso-acetoacetate precipit. $HNO_3/HClO_4$ redissolution; $1 \cdot 10^{13}$ n/cm^2 · s, 5–7 days irradiat.		20		Singh & Sawant (1987)
GC-ECD	HNO_3 digestion; urea; HCl reduction; toluene extraction; 1,2-diamino-4-nitrobenzene or 1,2-diamino-3,5-dibromobenzene; toluene extraction	5 ng	1·7	94–106	Shimoishi (1976) Tôei & Shimoishi (1981)
GC-ECD	$HNO_3/Mg(NO_3)_2$ digestion; HCl reduction; urea; 1,2-diamino-4-nitrobenzene; toluene extraction	5 ng/g			Stijve & Philippossian (1978)
GC-ECD	HNO_3 digestion; urea; HCl reduction; 4-nitro-*o*-phenylenediamine; benzene extraction; $MgSO_4$/Florisil cleanup	0·19 ng/g	3·4	75–90	Cappon & Smith (1978)
GC-ECD	$HNO_3/HClO_4$ digestion; HCl reduction; 4-trifluoromethyl-*o*-phenylenediamine; toluene extraction	5			Dilli & Sutikno (1984*a*)

thione peroxidase in mammals, a cellular form (c-GSHPx) and an extracellular or plasma form (p-GSHPx) (Broderick *et al.*, 1987; Maddipati & Marnett, 1987; Takahashi *et al.*, 1987; Avissar *et al.*, 1989*a*,*b*). The two enzymes have different affinities for glutathione and hydroperoxides. Both p-GSHPx and c-GSHPx have four Se molecules, interact with lipid peroxides and H_2O_2, and are the products of two different genes (Takahashi *et al.*, 1990; Avissar *et al.*, 1991). Thus, most, if not all, GSH-Px activity in milk is due to the p-GSH-Px form of the enzyme (Avissar *et al.*, 1991).

Levels in human milk

Table 2 shows the mean and range of Se concentrations in human milk from different parts of the world, also indicating, the number of samples analyzed, analytical method, some important descriptions and approximate year of the study. Most authors determine total Se levels because the normal sample treatment changes the initial composition of the milk. Studies in human milk from Japan (Shimoishi, 1976; Tôei & Shimoishi, 1981) determine the Se (VI) species, indicating that they constitute 30% of the total Se. The unit of concentration most used is μg/litre, although others have been used, such as pmol/g (Mangels *et al.*, 1990), ng/litre (Higashi *et al.*, 1983), μg/ml (Shimoishi, 1976; Tôei & Shimoishi, 1981), ng/g wet weight (Binnerts, 1979; Clemente *et al.*, 1982; Robberecht *et al.*, 1985; Tamari *et al.*, 1990, 1991) or dry weight (Lombeck *et al.*, 1977, 1978; Binnerts, 1979; Polkowska-Motrenko *et al.*, 1982; Kumpulainen *et al.*, 1983*a*), μg/g wet weight (Norheim *et al.*, 1983), μmol/litre (Koh & Benson, 1983). However, all concentrations were converted to μg/litre by using a density of 1·034 (Iyengar, 1982) or a mean dry-to-wet ratio of 0·12 (Cross *et al.*, 1978; Lombeck *et al.*, 1978; Iyengar, 1982).

Mature human milk can exhibit a wide variation in Se content due to geographical location. Shearer and Hadjimarkos (1975) have carried out an important study in 17 states across the USA, observing significantly higher concentration levels in high Se areas such as South Dakota compared to lower Se areas such as Ohio. Also, it was found that breast milk in a high Se area contained 283 μg Se/kg which can provide 220 μg Se/day for infants within the first year of age and is around 90 times the Se-intake supplied by breast milk in the Keshan disease area, where the Se concentration averaged 2·6 μg Se/kg (Keshan Disease Research Group, 1979*a*,*b*; Yang *et al.*, 1989). In 26 lactating women and their infants from the Kathmandu valley of Nepal, Se daily intake is considered the second-lowest reported in the world. However, the concentrations in maternal and infant plasma, and breast milk are below normal (Reynolds *et al.*, 1986). Kumpulainen *et al.* (1983*b*, 1984) suggest that maternal dietary Se intakes may be insufficient to maintain breast-milk Se concentrations at adequate levels for infants because Finland is a country with low-Se soils. Although some authors (Levander *et al.*, 1981, 1987; Higashi *et al.*, 1983) did not find significant correlations between Se levels in breast milk and dietary Se intakes, others (Shearer & Hadjimarkos, 1975; Kumpulainen *et al.*, 1985; Yang *et al.*, 1989) claimed that the Se content in human milk reflected a different Se intake via food.

Most authors indicate that human milk Se concentrations are dependent on the maternal Se intake; consequently, Se in human milk must also be dependent on the Se status. Thus, correlational analyses were performed between maternal indices of Se status and milk indices. Strong positive relationships were observed between maternal plasma (Levander *et al.*, 1981; Mannan & Picciano, 1987), serum (Higashi *et al.*, 1983; Kumpulainen *et al.*, 1985) or whole blood (Williams, 1983) Se concentrations and Se in milk. Plasma activity of GSH-Px was also positively correlated with both milk Se concentration and activity of GSH-Px (Mannan & Picciano, 1987). However, erythrocyte Se content did not correlate with milk Se concentrations (r = 0·23, p:NS) (Mannan & Picciano, 1987).

Some authors (Levander *et al.*, 1987) indicated that there was a weak (r = 0·38) but statistically significant ($p < 0·025$) correlation between maternal plasma and milk. In contrast, other investigators found that the level of Se in serum (Higashi *et al.*, 1983) or plasma (Levander *et al.*, 1981) of lactating women was unrelated to the Se content of their milk. The ability to demonstrate a correlation between blood and breast-milk Se levels may be determined in part, by the form of dietary Se ingested by the mothers (Levander *et al.*, 1987).

Another important factor that seems to influence Se content in milk is the state of lactation. Thus, the mean content found in USA (18 μg/litre) was lower than in North-West Germany (28 μg/litre). This could be due to the different state of lactation (Lombeck *et al.*, 1978) and/or different dietary Se intake. The 241 American women donating milk samples were from 17 to 869 days postpartum, with a median duration of 183 days, while most (88%) of the samples of mature milk from German women were collected from 11 to 60 days postpartum because of the usually short lactation time in this area (Lombeck *et al.*, 1978). Mature human milk exhibited a Se content very much lower than that observed in colostrum milk (Grimanis *et al.*, 1978; Lombeck *et al.*, 1978; Smith *et al.*, 1982; Higashi *et al.*, 1983; Robberecht *et al.*, 1985; Tamari *et al.*, 1991). Also, the available data reveal a strong downward trend in breast milk Se concentration during the first 10 days of lactation (Millar & Sheppard, 1972; Grimanis *et al.*, 1978; Higashi *et al.*, 1983; Varo *et al.*, 1984; Tamari *et al.*, 1990, 1991, 1992; Yuzo & Mohri, 1991). Cumming *et al.* (1983) showed that, in a group of lactating Australian women, the mean plasma/milk selenium ratio was 6·9 ± 1·83. This ratio increases slightly with the progression of lactation; while the plasma concentration remains constant the milk concentration declines. Lombeck *et al.* (1978) have shown an inverse relationship between the Se content and the

Table 2. Selenium levels (μg/litre) in human milk

Geographical location	Date (year)	Anal. method[a]	Mean (μg/litre) (min–max)	N°	Description[b]	Ref.
EUROPE						
Austria (Styria)	1988–91	HG-AAS	8·3 ± 3·0	34	Mature milk	Tiran *et al.* (1992)
Belgium	1983	HG-AAS	14·3 ± 4·7 (6·4–26·3)	24	Colostrum 0–3 days pp	Robberecht *et al.* (1985)
			11·9 ± 4·2 (5·3–18·1)	13	Transitory milk 5–7 days pp	
			12·3 ± 3·4 (6·5–17·1)	11	Transitory milk 8–10 days pp	
			9·1 ± 1·9 (6·5–12·3)	15	Mature milk 1 month pp	
			9·6 ± 3·3 (5·4–14·9)	9	Mature milk 2 months pp	
			9·3	1	Pooled milk	
Finland (Helsinki)	1976	EAAS	10·7 ± 1·6	13	1 month pp	Kumpulainen *et al.* (1983*b*)
			5·8 ± 1·2	13	3 months pp	
			5·6 ± 0·4	4	6 months pp	
Finland (Helsinki)	1980	EAAS	11·8	—	1 month pp	Kumpulainen *et al.* (1984)
			10·0	—	3 months pp	
Finland	1982	EAAS	6·0 ± 0·5	—	Dried milk	Kumpulainen *et al.* (1983*a*)
Germany (Düsseldorf)	1976	INAA	14·9 (11·4–18)	3	≥15 days pp	Lombeck *et al.* (1977)
Germany (Düsseldorf)	1978	INAA	77·9 (60·8–100·4)	3	Colostrum 2–3 days pp	Lombeck *et al.* (1978)
			28·4 (15·1–48·9)	25	Transitory milk 4–10 days pp	
			26·7 (10·4–50·1)	44	Mature milk 11–173 days pp	
Germany	1986	SPF	17·8	—	10 days pp	Oster *et al.* (1986)
Greece (Athens)	1973	SPF	21 ± 1	24	29–195 days pp	Hadjimarkos & Shearer (1973)
Greece	1978	INAA	48 (33–69)	15	Colostrum 0–3 days pp	Grimanis *et al.* (1978)
			16 (10–20)	15	Transitory milk 4–10 days pp	
			15 (14–22)	5	Mature milk 1 month pp	
Italy	1982	INAA	12·9 ± 0·9 (≤0·9–47·9)	20	≥15 days pp	Clemente *et al.* (1982)
Spain (Barcelona)	1981	SPF	11·4 ± 2·9 (9–18)	8	3–10 days pp	Farré *et al.* (1981)
UK (Glasgow)	1978	—	31 ± 10	25	—	Cross *et al.* (1978)
Yugoslavia (Ljubljana)	1982	RNAA	(7·4–14·5)	10	—	Polkowska-Motrenko *et al.* (1982)
Yugoslavia (Ljubljana)	1983	RNAA	11·5 ± 3·6 (5·7–16·7)	27	0–14 days pp	Kosta *et al.* (1983)
AMERICA						
USA (Arizona, Douglas)	1974	SPF	20 ± 1 (11–27)	14	22–344 days pp 18–32 yr old	Shearer & Hadjimarkos (1975)
USA (Calif., Sta Barbara)		SPF	18 ± 2 (10–32)	14	28–360 days pp 22–35 yr old	
USA (Colorado, Pueblo)		SPF	15 ± 1 (12–20)	15	86–648 days pp 19–33 yr old	
USA (Connect., Bristol)		SPF	15 ± 1 (8–23)	15	29–425 days pp 19–29 yr old	
USA (Georgia, Athens)		SPF	18 ± 1 (12–25)	11	28–360 days pp 20–39 yr old	

continued

Table 2—*continued*

Geographical location	Date (year)	Anal. method[a]	Mean (μg/litre) (min–max)	Nº.	Description[b]	Ref.
AMERICA—contd.						
USA (Illinois)	1981	GC-ECD	41·2 ± 17·3	8	Colostrum 0–3 days pp	Smith *et al.* (1982)
			18·0 ± 3·8	8	1 month pp	
			15·7 ± 4·6	8	2 months pp	
			15·1 ± 5·8	8	3 months pp	
			15·7 ± 4·9	20	Fore milk 2 weeks pp	
			14·4 ± 1·6	20	Fore milk 1 month pp	
			14·1 ± 3·2	20	Fore milk 2 months pp	
			13·9 ± 3·2	20	Fore milk 3 months pp	
			16·3 ± 4·9 (8–34)	72	Average fore milk	
			16·3 ± 4·8	20	Hind milk 2 weeks pp	
			15·2 ± 3·2	20	Hind milk 1 month pp	
			15·9 ± 3·4	20	Hind milk 2 months pp	
			16·4 ± 3·1	20	Hind milk 3 months pp	
			16·2 ± 5·4	16	Morning milk	
			16·6 ± 4·8	16	Midday milk	
			15·8 ± 4·6	16	Evening milk	
USA (Illinois)	1984–85	GC-ECD	16·8 (11·5–27·3)	10	4–8 weeks pp 30 ± 5·6 years old	Mannan & Picciano (1987)
			15·6 ± 0·4	10	Fore milk	
			18·1 ± 0·6	10	Hind milk	
USA (Illinois)	1986	GC-ECD	15·2 ± 0·6	10	—	Debski *et al.* (1987)
			15·1 ± 0·9	10	Skimmed milk	
			11·0 ± 0·5	10	Dialyzed milk	
USA (Indiana, Evansville)	1989	SPF	23 ± 4	12	0–2 months pp	Litov *et al.* (1989)
USA (Iowa, Iowa City)	1973	SPF	20 ± 1 (15–24)	15	40–83 days pp 18–31 yr old	Hadjimarkos & Shearer (1973)
USA (Maryland)	1981	—	20 ± 4	23	1 month pp	Levander *et al.* (1981)
			15 ± 3	23	3 months pp	
			15 ± 4	23	6 months pp	
USA (Maryland)	1986	SPF	20 ± 1	10	1 month pp	Levander *et al.* (1987)
			15 ± 1	10	3 months pp	
			15 ± 1	10	6 months pp	
USA (Missouri, Rolla)	1974	SPF	20 ± 1 (13–28)	15	22–540 days pp 22–37 yr old	Shearer & Hadjimarkos (1975)
USA (Montana, Billings)			21 ± 1 (16–27)	10	42–390 days pp 24–30 yr old	
USA (New York, Syracuse)			15 ± 1 (10–19)	15	23–869 days pp 25–39 yr old	
USA (New York)	1980	—	56	—	Colostrum	Amin *et al.* (1980)
			31	—	Colostrum	
USA (New York, Rochester)	1989–90	SPF	13·1	3	1–8 months pp	Avissar *et al.* (1991)
USA (Ohio, Akron)	1974	SPF	13 ± 1 (7–17)	15	20–353 days pp 23–42 yr old	Shearer & Hadjimarkos (1975)
USA (Oklahoma, Norman)			16 ± 1 (9–26)	14	43–630 days pp 20–36 yr old	
USA (Oregon, Portland)	1973	SPF	21 ± 3 (13–53)	15	42–150 days pp 17–44 yr old	Hadjimarkos & Shearer (1973)

Table 2—*continued*

Geographical location	Date (year)	Anal. method[a]	Mean (μg/litre) (min–max)	Nº.	Description[b]	Ref.
AMERICA—contd.						
USA (Pennsylvania, State College)	1974	SPF	21 ± 1 (12–26)	15	65–363 days pp 22–33 yr old	Shearer & Hadjimarkos (1975)
USA (South Dakota, Sioux Falls)			28 ± 3 (17–60)	15	112–389 days pp 21–41 yr old	
USA (Texas, Corpus Christi)			16 ± 1 (9–22)	15	24–480 days pp 20–31 yr old	
USA (Utah, Salt Lake City)			22 ± 3 (14–52)	14	17–390 days pp 21–32 yr old	
USA (Utah, Salt Lake City)	1989	SPF	25 ± 5	10	0–2 months pp	Litov *et al.* (1989)
USA (Washington DC)	1989	IDMS	204 ± 13 (151–327)	6	74 ± 5 days pp 29 ± 2 yr old	Mangels *et al.* (1990)
USA (Wyoming, Cheyenne)	1974	SPF	16 ± 1 (10–26)	14	37–704 days pp 17–38 yr old	Shearer & Hadjimarkos (1975)
ASIA						
Japan (Okayama)	1975–80	GC-ECD	45 ± 38 (10–83)	3	—	Robbins & Caruso (1979); Shimoishi (1976); Tôei & Shimoishi (1981)
Japan (Kyoto)	1982	—	22·5 ± 4·2	13	Mature milk	Hojo (1982)
Japan	1983	SPF	(35–152)	7	Colostrum (0–3 days pp)	Higashi *et al.* (1983)
			(15–79)	10	Transitional milk (4–10 days pp)	
			(9–39)	9	Mature milk (1 month pp)	
			(6–28)	8	(3 months pp)	
			(9–33)	7	(5 months pp)	
			21	34	Average content without colostrum	
Japan	1986	SPF	22·5	—	Mature milk	Hojo (1986*b*)
Japan	1990	SPF	19·6	—	Colostrum (2 days pp)	Tamari *et al.* (1990)
			0·8	—	Milk, 5 days pp	
Japan	1991	SPF	28·4	—	Colostrum	Tamari *et al.* (1991, 1992)
			8·7	—	Mature milk (7–171 days pp)	
Japan	1991	SPF	29·7 ± 10·5	8	Colostrum	Yuzo & Mohri (1991)
			18·9 ± 9·4	8	Transitional milk (4–7 days pp)	
			10·8 ± 2·7	8	Mature milk (7–21 days pp)	
OCEANIA						
Australia	1982	INAA	11·6 ± 1·9* (9·7–29)	14	8–23 weeks pp	Cumming *et al.* (1983)
Kensington	1984	GC-ECD	8	1	Healthy	Dilli & Sutikno (1984*a*)
New Zealand	1983	—	7·6	—	1 month pp	Williams (1983)

[a] GC-ECD: Gas-chromatography with electron capture detection; IDMS: Isotope dilution mass spectrometry.
[b] pp: Postpartum.
*pmol Se/g.

time postpartum; however, other authors (Shearer & Hadjimarkos, 1975) have indicated that this correlation was very weak ($r = -0{\cdot}13$, $p < 0{\cdot}05$). Another author (Hojo, 1986*a*) showed that both GSH-Px and Se contents of breast milk decreased with increasing time of lactation and reached a plateau one month postpartum. This sequential change was not due to the Se intake of the mothers, as reflected in urinary Se content. This is in accordance with the values in serum (Lombeck *et al.*, 1978; Kumpulainen *et al.*, 1987) and whole blood (Mackenzie *et al.*, 1978) Se concentrations of children. Also a strong decrease in breast-milk Se during the first and third months of lactation has been observed in lactating women from Finland (≈30 μg Se/day) (Kumpulainen *et al.*, 1983*b*) and Belgium (Robberecht *et al.*, 1985). However, in mature human milk from the

Table 3. Selenium levels (μg/litre) in cow's milk

Geographical location	Date (year)	Anal. method[a]	Mean (min–max)	Nº.	Description	Ref.
EUROPE						
Finland	1977	HG-AAS	7·89 ± 1·2	16	Dairy cows	Varo & Koivistoinen (1981)
	1977		3·48 (3·48–4·64)	6	Dairy cows (standardized)	
	1980		8·12 (6·96–9·28)	6	Dairy cows (untreated)	
Germany (Düsseldorf)	1976	INAA	10·2 ± 2·55 (7·8–12·9)	3	Dairy cows	Lombeck *et al.* (1977)
Germany (Düsseldorf)	1978	INAA	23·2 (16·2–35·2)	45	Dairy cows	Lombeck *et al.* (1978)
Germany	1986	—	(6·8–7·2)	—	Dairy cows	Oster *et al.* (1986)
Norway (Oslo)	1979	SPF	10·6 (7·7–11·6)	13	Dairy cows	Karlsen *et al.* (1981)
Norway	1983	EAAS	10·1 ± 2·5 (7·2–15·3)	10	Cows	Norheim *et al.* (1983)
The Netherlands	1973	INAA	7·6 ± 0·82 (7·5–13·3)	5	Soil type marine clay	Binnerts (1979)
			3·9 ± 0·30 (3·4–5·45)	5	Soil type sand and peat	
			5·1 ± 0·63 (5·2–7·54)	6	Soil type mixed	
The Netherlands	1989	SPF	16·5 ± 1·3 (14·5–18·4)	7	Winter milk	Koops *et al.* (1989)
		EAAS	15·5 (14·5–17·4)	7		
		SPF	10·3 ± 0·5 (9·7–10·6)	7	Summer milk	
		EAAS	9·7 (7·7–13·5)	7		
AMERICA						
Canada (British Columbia)	1979	SPF	28	8	Holstein cows	Fisher *et al.* (1980)
USA (Florida)	1980	—	(8–13)	—	Beef cattle Se supplement.	Ammerman *et al.* (1980)
USA (Illinois)	1987	GC-ECD	9·6 ± 0·4	10	Holstein cows (whole milk)	Debski *et al.* (1987)
			9·5 ± 0·3	10	Holstein cows (skimmed milk)	
			7·3 ± 0·3	10	Holstein cows (dialyzed milk)	
USA (Indiana)	1977	—	(14–23)	—	Hereford cows Se supplement 2–3 days postpartum	Perry *et al.* (1977)
			(16–21)	—	Hereford cows Se supplement 3 months postpartum	
USA (Ohio)	1978	SPF	8 ± 1·9	5	Jersey and Holstein cows	Conrad & Moxon (1979)
USA (Ohio)	1981	—	5	—	Beef cattle	Moxon (1981)
USA (South Dakota)	1977	SPF	64 ± 13 (45–80)	8	Dairy cows (December)	Olson & Palmer (1984)
	1978		53 ± 20 (32–88)	8	Dairy cows (January)	
			46 ± 7 (36–58)	8	Dairy cows (May)	
			64 ± 10 (54–80)	8	Dairy cows (September)	
			78 ± 27 (61–138)	8	Dairy cows (December)	

Table 3—*continued*

Geographical location	Date (year)	Anal. method[a]	Mean (min–max)	Nº.	Description	Ref.
ASIA						
India (Bombay)	1987	INAA	1·5 ± 3	—	Dairy cows	Singh & Sawant (1987)
Japan	1980	GC-ECD	(21–27) Se_T (12–17) Se (VI)	3	Dairy cows	Tôei & Shimoishi (1981)
Japan	1981	—	64	—	Dairy cows	Munnehiro *et al.* (1981)
Japan (Kyoto)	1982	SPF	23	—	Dairy cows	Hojo (1982)
Japan	1990	SPF	17·4 ± 3·6	13	—	Tamari *et al.* (1990)
OCEANIA						
Australia	1982	SPF	0·2 ± 0·01*	4	Raw milk	Koh & Benson (1983)
New Zealand	1980	SPF	7·2	—	—	Grant (1981)

[a] GC-ECD: Gas-chromatography with electron capture detection.
* μmol Se/litre.

USA (Shearer & Hadjimarkos, 1975; Smith *et al.*, 1982) or Japan (Higashi *et al.*, 1983), with an average dietary intake of 80 and 88 μg/day respectively, the concentration of Se does not usually decline significantly with the advancing stages of lactation. Maternal body reserves and/or low dietary Se intake may not have been sufficient to maintain the Se level of breast milk (Kumpulainen *et al.*, 1983*b*).

Variations in Se concentrations of human milk can occur during the same feed. Se content in hind milk was found to be greater than fore milk at two and three months postpartum (Smith *et al.*, 1982) and in the first four months also (Mannan & Picciano, 1987). However, no significant differences were found in human milk samples of ≤1 month taken before, during and after feeding (Millar & Sheppard, 1972; Smith *et al.*, 1982). Maternal stature, maternal weight or infant's birth weight contribute to the variation in elemental concentration in milk although the contributions were small in all cases (Yoshinaga *et al.*, 1991). There was no correlation between Se levels and the ages of the individual donors (Shearer & Hadjimarkos, 1975).

Levels in other commercial milk adapted to human milk

Selenium concentration in milk from different animal species decreases in the order: human, sheep > goat > cow (Debski *et al.*, 1987). The Se contents in commercial milks adapted to human milk, or to cow's milk and other derivatives have been reported showing the results in ng/g dw (Lombeck *et al.*, 1977, 1978), μg/litre (Shimoishi, 1976; Farré *et al.*, 1981; Hojo, 1982), μg/kg (Bruhn & Franke, 1977; Charlot *et al.*, 1989), or ng Se/kcal (Roekens *et al.*, 1985). Although there are exceptions (Higashi *et al.*, 1982; Hatano *et al.*, 1985), most authors (Lombeck *et al.*, 1977, 1978; Farré *et al.*, 1981; Smith *et al.*, 1982; Hojo, 1986; Debski *et al.*, 1987; Tamari *et al.*, 1991, 1992) reported that the Se content of human milk is significantly greater than in the available milk formulas for infants. In this sense, the Se content of infant formulas marketed in the USA is approximately 40% of that of mature human milk (Smith *et al.*, 1982). Also, the average Se content of 107 samples of 10 different cow's milk infant formulas from Germany was less than 33% of that of mature human milk (Lombeck *et al.*, 1978). However, several authors (Lombeck *et al.*, 1977; Tamari *et al.*, 1990; Hojo, 1982) did not find significant differences between the values of mature human milk and of cow's milk (Table 3). Due to the fact that many Se compounds in milk are quite volatile, processing by hot-air treatment could reduce the Se content of cow's milk with increasing temperature and time of heating (Morris & Levander, 1970; Lombeck *et al.*, 1977). So, Hojo (1986*b*) found losses of Se amounted to 11·1% at 210°C for 25 min. On the other hand, mean levels of Se (μg/litre) decreased in the sequence: pasteurized cow's milk (28·4) > raw cow's milk (23·1) > mature human milk (22·5) > milk-based infant formula (6·6) (Hojo, 1986*b*). Lombeck *et al.* (1980) estimated the Se content of samples of raw cow's milk, ultra-high temperature sterilized milk, and skimmed milk. There was no statistically significant differences in comparison with the respective pasteurized milk samples from the same geographic region. Absence of GSH-Px activity in pasteurized milk and infant formula results from the heating process in their preparation (Hojo, 1986*b*). In one study (Zabel *et al.*, 1978), infant formulas, not generally supplemented with Se, varied widely in Se content, depending upon their source of ingredients. Also, Se content of nonfat dry milk varies greatly depending on the geographic origin of the milk (Varo *et al.*, 1984). According to the latter, the greater Se content in cow's milk was found in South Dakota, a typical seleniferous area (Olson & Palmer, 1984). On the other hand, the areas which correspond with low Se contents in milk may in fact be Se-deficient (Binnerts, 1979).

There are other factors that can produce some variations in the Se content of cow's milk. Thus, untreated cow's milk obtained in July contained higher levels of Se than that obtained in November (Hojo, 1982). However, in processing plants in South Dakota state, the

Table 4. Estimated daily intake of selenium (μg/day) for infants

Geographical location	Data (year)	Subjects	Feed type	Mean (min–max)	Ref.
EUROPE					
Belgium	1983	Boys, 3 months	Breast milk	8·1	Tiran *et al.* (1992)
		Girls, 3 months		7·1	
Belgium	1984	1 month	Breast milk	6·1 (3·8–10·4)	Roekens *et al.* (1985)
		3 months		7·2 (4·5–12·4)	
		6 months		8·6 (5·4–14·8)	
		3 months	Bottle-fed cow's milk	9·0	
		1 month	Milk-based formula	3·0 (0·4–10·9)	
		3 months		3·5 (0·5–12·9)	
		6 months		4·2 (0·6–15·4)	
		1 month	Milk infant formula therapeutic use	5·7 (0·6–15·9)	
		3 months		6·7 (0·7–18·9)	
		6 months		8·0 (0·8–22·5)	
		1 month	Processed cow's milk	7·6 (6·1–12·8)	
		3 months		9·0 (7·2–15·2)	
		6 months		10·8 (8·6–18·1)	
Finland (Helsinki)	1976	1 month, n = 10	Breast milk	8·0 ± 1·8	Kumpulainen *et al.* (1983*b*)
		3 months, n = 10		4·7 ± 1·1	
Finland (Helsinki)	1981–82	4–12 months n = 16	Milk infant formula (Se supplemented)	16	Kumpulainen *et al.* (1987)
Germany (Düsseldorf)	1976–77	2 months	Cow's milk infant formula	7·8	Lombeck *et al.* (1978)
	1978	2 months	Breast milk	22·4	
Germany	1986	3·5 kg of weight	Breast milk	12	Oster *et al.* (1986)
			Milk infant formula	< 3·5	
			Cow's milk	5	
Spain (Barcelona)	1981	1 week	Breast milk	2·39	Farré *et al.* (1981)
		1st week	Milk infant formula	2·34	
		2nd week	Breast milk	3·19	
			Milk infant formula	3·13	
		3–4 weeks	Breast milk	3·19	
			Milk infant formula	3·90	
		2nd month	Breast milk	3·23	
			Milk infant formula	6·25	
		3rd month	Breast milk	4·18	
			Milk infant formula	8·65	
		4th month	Breast milk	4·53	
			Milk infant formula	9·96	
			Bottle-fed cow's milk	6·94	
		5–6 months	Breast milk	4·53	
			Milk infant formula	10·27	
			Bottle-fed cow's milk	6·78	
		7–9 months	Breast milk	—	
			Milk infant formula	9·66	
			Bottle-fed cow's milk	6·82	
		10–12 months	Breast milk	—	
			Milk infant formula	7·33	
			Bottle-fed cow's milk	5·60	

Table 4—*continued*

Geographical location	Data (year)	Subjects	Feed type	Mean (min–max)	Ref.
EUROPE—contd.					
UK (Scotland)	1978	3 months	Breast milk	35	Cross *et al.* (1978)
			Milk infant formula	18	
AMERICA					
USA	1978	0–6 months	Milk based diets	8·5	Zabel *et al.* (1978)
USA (Illinois)	1981	3 months	Breast milk	10·08 ± 2·96	Smith *et al.* (1982)
			Milk infant formula	7·22 ± 1·26	
USA (Maryland)	1986	1 month	Breast milk	10	Levander *et al.* (1987)
		3 months		12	
		6 months		13	
—	1990	8–12 months	Formula-fed	31	Gropper *et al.* (1990)
		n = 26	Cow's milk	34	
ASIA					
China	1985–86	—	Breast milk	11·8	Yang *et al.* (1989)
(low Se area)					
(medium Se area)		—		24·3	
(high Se area)		—		94·6	
Japan	1983	5 months	Breast milk	17	Higashi *et al.* (1983)
Japan	1991	0–4 days	Colostrum	17	Tamari *et al.* (1991, 1992)
		>1 month	Breast milk	8	
Japan	1991	—	Formula-fed	(2–3)	Tamari *et al.* (1991)
Japan	1986	3 months	Breast milk	21·0	Hojo (1986*b*)
			Pasteur. cow's milk	18·9	
			Raw cow's milk	15·0	
			Formula-fed	5·4	
Japan	1991	—	Formula-fed	(3–6)	Tamari *et al.* (1992)
Japan	1991	—	Colostrum	(10–15)	Yuzo & Mohri (1991)
			Formula-fed	(3–5)	
OCEANIA					
New Zealand	1972	1 month	Breast milk	5	Millar & Sheppard (1972)
			Bottle-fed cow's milk	2	

highest values were obtained in winter and the lowest in summer (Olson & Palmer, 1984). The Se concentration in colostral milk (0·13–0·21 μg/g dry weight) was determined in cows with or without retained placenta (Bostedt & Schramel, 1981) and in healthy cows (Koller *et al.*, 1984). The effect of mastitis on the Se content of cow's milk was studied (Sarudi *et al.*, 1989; Osama *et al.*, 1992). The concentration in milk increased with the presence of mastitis, and also with increasing severity of mastitis (Sarudi *et al.*, 1989), but serum Se levels remained within the normal range (Osama *et al.*, 1992).

SELENIUM INTAKE FOR LACTATING INFANTS

As can be seen in Table 4, there are great variations of the estimated daily intakes of Se in lactating babies from different geographical areas. These values in general are very small compared to those of adults, which amount to about 56 μg/day in New Zealand (Watkinson, 1974), to 88·3 μg/day in Japan (Sakurai & Tsuchiya, 1975) and 197 μg/day in Canada (Thompson *et al.*, 1975). The daily Se intakes of infants, as calculated from daily breast milk consumption, averaged 2·5, 11·8, 24·3, and 94·6 μg/day in Keshan-disease, low, medium, and high Se-areas in China, respectively (Levander, 1987; Yang *et al.*, 1989). As a consequence of decrease in dietary intake, a significant decrease in Se in neonates from Helsinki was observed (Kumpulainen *et al.*, 1983*b*; Alfthan, 1986). Dietary Se intakes of Finnish (Kumpulainen *et al.*, 1983*b*) and Belgian (Robberecht *et al.*, 1985) breast-fed infants are considerably lower than the lowest level of 'safe and adequate' intake of 10 μg/day proposed by the National Research Council. But all infants were healthy, gaining weight and height according to the norms of typical Finnish infants (Vuori & Kuitunen, 1979).

On the other hand, infants fed human milk have a higher Se intake than those fed commercially available formula milk or baby foods (Lombeck *et al.*, 1977; Cross *et al.*, 1978; Smith *et al.*, 1982; Oster *et al.*, 1986; Gropper *et al.*, 1990; Tamari *et al.*, 1991). In the case of baby foods, it is surprising because cereals are widely fed as first solid foods, and cereals are considered important sources of Se. However, Se in cereals is lost (7–78%) after dry heating (Morris & Levander, 1970; Higgs *et al.*, 1972) which could explain the lower Se intakes in infants fed baby foods. Therefore, dietary Se intake (μg/day) of three-month-old Japanese infants fed on infant formula and various milks decreased in the order: human milk (21·0) > pasteurized cow's milk

(18·9) > raw cow's milk (15·0) > infant formula (5·4). So, a two-month-old German infant on cow's milk infant formula alone receives about 7·8 μg Se/day in its food, while a breast-fed infant receives about 22·4 μg Se/day (Lombeck *et al.*, 1978). The Se intake of infants fed with commercially available infant formulas and some vegetables is approximately 2–6 μg/day (Lombeck *et al.*, 1977). Selenium intake of infants fed on the formula seems to be at the intermediate level between Se deficiency and adequate amounts (Yuzo & Mohri, 1991).

These higher intakes in the breast-fed (BF) infant were reflected in higher serum Se compared to a formula-fed (FF) infant. So, at one to five weeks of age, the plasma Se content in BF infants was higher than that in cord blood, and in FF infants it was similar to the level in cord blood. A significant positive correlation ($r = 0{\cdot}42$, $p < 0{\cdot}05$) was found between the Se intake of infants and their serum Se concentration at three months (Smith *et al.*, 1982). Serum Se concentrations were significantly higher in BF infants, than in FF infants. Hatano *et al.* (1984, 1985) and Gropper *et al.* (1990) observed significantly lower concentrations of plasma Se in FF than in BF infants, although the Se intake was almost the same in both groups. Consequently, the Se compounds in breast milk seem to be more biologically available for infant nutrition than those in formulas (Hatano *et al.*, 1985; Kumpulainen *et al.*, 1987; Tamari *et al.*, 1991; Yuzo & Mohri, 1991).

CONCLUDING REMARKS

Mature human milk has a Se content lower than transitory milk, and transitory milk lower than colostrum. This fact could be due to differences in protein content, owing to the fact that most of the fraction of Se in milk is associated with the protein fraction.

It can be confirmed that Se in milk, and therefore Se intake and status of newborns, is largely a function of the Se intake of the mother. However, there must be other influential factors such as the form of bioavailability of Se in the diet, as well as interactions with other nutrients.

Decrease with time of Se concentration in mature human milk has been observed in low-Se areas. Body reserves do not seem to be sufficient to maintain the Se level of breast milk.

Human milk has higher Se levels than milk formulas for infants, perhaps due to losses in the latter by processing. Also, Se compounds in breast milk seem to be more biologically available for infants than for those in formulas.

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