MINOR AND TRACE ELEMENTS IN BREAST MILK

Report of a Joint WHO/IAEA Collaborative Study

WORLD HEALTH ORGANIZATION
GENEVA

INTERNATIONAL ATOMIC ENERGY AGENCY
VIENNA

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The World Health Organization is a specialized agency of the United Nations with primary responsibility for international health matters and public health. Through this organization, which was created in 1948, the health professions of some 165 countries exchange their knowledge and experience with the aim of making possible the attainment by all citizens of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life.

By means of direct technical cooperation with its Member States, and by stimulating such cooperation among them, WHO promotes the development of comprehensive health services, the prevention and control of diseases, the improvement of environmental conditions, the development of health manpower, the coordination and development of biomedical and health services research, and the planning and implementation of health programmes.

These broad fields of endeavour encompass a wide variety of activities, such as developing systems of primary health care that reach the whole population of Member countries; promoting the health of mothers and children; combating malnutrition; controlling malaria and other communicable diseases including tuberculosis and leprosy; having achieved the eradication of smallpox, promoting mass immunization against a number of other preventable diseases; improving mental health; providing safe water supplies; and training health personnel of all categories.

Progress towards better health throughout the world also demands international cooperation in such matters as establishing international standards for biological substances, pesticides and pharmaceuticals; formulating environmental health criteria; recommending international nonproprietary names for drugs; administering the International Health Regulations; revising the International Classification of Diseases, Injuries, and Causes of Death; and collecting and disseminating health statistical information.

Further information on many aspects of WHO's work is presented in the Organization's publications.

Preface

This volume completes a series of publications describing a multinational study on breast-feeding which was initiated by the World Health Organization in 1973. Results of the first phase were published in 1981 in a book entitled *Contemporary patterns of breast-feeding* (*1*). The second phase of the study, which was concerned specifically with the volume and composition of breast milk, was published in 1985 (*2*) and contained data on concentrations of protein, non-protein nitrogen, lactose, fat, lactalbumin, lactoferrin, vitamin A, vitamin C, and some pesticides. Results of analyses for minor and trace elements in milk samples collected from the same study groups in Guatemala, Hungary, the Philippines, Sweden and Zaire and from a study group in Nigeria are presented here.

This work deliberately focused on the study of trace elements, since it was considered that there was a lack of reliable data for the concentration of many such elements in human milk. The elements selected for study included all the known essential trace elements, with the exception of silicon, and some important toxic trace elements. Calcium, chlorine, magnesium, phosphorus, potassium and sodium were also included since, like many of the trace elements, they are biologically essential, and their analysis could be carried out by similar means; further, there are important interactions between some of these elements that are potentially of interest. Altogether, therefore, 24 elements were included in this study, namely: antimony, arsenic, cadmium, calcium, chlorine, chromium, cobalt, copper, fluorine, iodine, iron, lead, magnesium, manganese, mercury, molybdenum, nickel, phosphorus, potassium, selenium, sodium, tin, vanadium and zinc.

Published values for most, if not all, of these elements can be found in the scientific literature, and it is therefore legitimate to question why it was necessary to conduct this study at all. The explanation is simply that some of the analyses are extremely difficult to perform properly, and it is only in recent years, and in very few laboratories, that reliable results have begun to be obtained. Consequently, the scientific literature is full of inconsistent data and it is generally impossible to decide *a priori* whether the differences are real (representing biological or geographical variability) or whether they are simply the result of analytical error. The principal aim of this study was, therefore, to obtain reliable data on the quantities of minor and trace elements present in human milk. A second objective was to find out whether the

concentrations of these elements varied significantly with the socioeconomic group or geographical origin of the mothers, and indirectly with their nutritional status.

An important requirement in such a programme is the development and use of suitable procedures for analytical quality assurance, the main components of which, as used in this study, comprise: (1) standardized procedures for the collection of samples; (2) the use of a single reference analytical laboratory for each element (thus eliminating interlaboratory systematic errors); and (3) the use of appropriate analytical reference materials (to provide some assurance of the reliability of the results reported by the reference laboratories).

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Contents

1. Trace elements in human nutrition

Trace elements have a variety of biochemical functions in all living organisms, and their presence in amounts that are too high or too low can have important consequences.

Among the numerous trace elements, 15 (arsenic, chromium, cobalt, copper, fluorine, iodine, iron, manganese, molybdenum, nickel, selenium, silicon, tin, vanadium and zinc) are currently thought to be essential for humans (though for some of them—arsenic, nickel, tin and vanadium—the only evidence comes from animal experiments).

Historically, the need for iron has been known since the seventeenth century. Similarly, the role of iodine as an essential component of human and animal health was recognized in about 1850. However, most of our knowledge of the remaining essential trace elements was acquired in this century, particularly since 1950. The roles played by these elements are numerous. In some cases they serve as constituents of vital biological molecules (such as iron in haemoglobin and iodine in thyroid hormones); in others they are either part of an enzyme system or exert their influence as co-factors for various reactions mediated by enzymes. Table 1 summarizes the biochemical roles and signs of deficiency in humans of the 15 essential trace elements.

Trace elements are known to play a particularly important role in growth and development. In animals, it has been demonstrated through extensive experiments that there is a need for an adequate supply of essential trace elements, such as copper, iron, manganese and zinc, for growth and development of the neonate (*3*, *4*). Deficiencies of these elements may result in poor growth, abnormal overall development, skin disorders, bone fractures and increased neonatal morbidity. In human subjects, copper, selenium and zinc deficiency syndromes have been reported during the last 20 years (*5*, *6*).

The young of all species are specially susceptible to the effects of trace element deficiencies. For example, iron deficiency impairs intellectual development in young children, and iodine deficiency has serious effects, both before and after birth, on mental development and physical growth. Similarly, serious growth retardation results

Table 1. Classification of essential trace elements

Element	Year of discovery of element's importance	Function	Deficiency signs in humans
Iron	17th century	Oxygen, electron transport	Anaemia
Iodine	1850	Constituent of thyroid hormones	Goitre, depression of thyroid function, cretinism
Copper	1928	Constituent of oxidative enzymes; interaction with iron; cross-linking of elastin	Anaemia, changes of ossification, possibly elevated serum cholesterol
Manganese	1931	Mucopolysaccharide metabolism; constituent of superoxide dismutase	Not known
Zinc	1934	Constituent of numerous enzymes involved in energy metabolism and in transcription and translation	Growth depression, sexual immaturity, skin lesions, depression of immunocompetence, change of taste acuity
Cobalt	1935	Constituent of vitamin B_{12}	Only as vitamin B_{12} deficiency
Molybdenum	1953	Constituent of xanthine, aldehyde and sulfide oxidases	Not known
Selenium	1957	Constituent of glutathione peroxidase; interaction with heavy metals	Endemic cardiomyopathy (Keshan disease) caused by selenium deficiency
Chromium	1959	Potentiation of insulin	Relative insulin resistance, impaired glucose tolerance, elevated serum lipids
Tin	1970	Not known	Not known
Vanadium	1971	Not known	Not known
Fluorine	1971	Structure of teeth, possibly of bones; possible growth effect	Increased incidence of caries, possible risk factor for osteoporosis
Silicon	1972	Calcification possible function in connective tissue	Not known
Nickel	1976	Interaction with iron absorption	Not known
Arsenic	1977	Not known	Not known

from zinc deficiency in infants and children, while adolescents may suffer from delayed sexual maturation.

In this context, infant nutrition, especially during the early stages of infancy, assumes special importance. Human milk, or a simulated version of it such as a milk formula product, is usually the only source of food for infants during the first months of life. It is therefore essential that it should contain all necessary nutrients in adequate amounts. This is particularly important for elements that are not stored by the fetus *in utero*. From this point of view one can distinguish two groups of elements: those such as copper and iron for which body stores are normally sufficient at birth to protect the infant from deficiency for 4–6 months, and those such as selenium and zinc, for which body stores are not extensive and which therefore need to be taken in sufficient quantities at all times to maintain optimal growth and development.

Spurred on by this kind of knowledge, many governments have started to specify recommended dietary intakes of minor and trace elements. Supplementation of human diets in general, and of infant diets in particular, with elements such as iron, iodine, and fluorine is already being promoted by national health authorities, and in at least one country (Finland) indirect supplementation with selenium (via fertilizer applied to farmland) has recently been started.

As far as infant foods are concerned, the main issue is whether milk formula products consumed by babies who are not breast-fed contain adequate levels of essential nutrients. A WHO Expert Committee report in 1973 (*7*) contained recommendations for levels of essential trace elements in milk formula, based on the levels found in human or cow's milk but noted that there was a need for additional information on the quantities of trace elements present in human milk if the recommendations were to be implemented successfully. This, therefore, was the principal aim of the study described in this report.

2. Methods

Sample collection

As outlined in the report on the second phase of this study (*2*), three groups of mothers were studied in each of the six countries participating in this project:

— urban well-to-do or economically advantaged mothers (group 1);
— urban poor or economically disadvantaged mothers (group 2); and
— rural mothers following a traditional way of life in families mostly dependent on subsistence agriculture and local marketing. (group 3).

The centres collaborating in the project were located in Guatemala, Hungary, Nigeria, the Philippines, Sweden, and Zaire. It was realized that, in some of these countries, the groupings indicated above would have little meaning, and therefore modifications to this general scheme were agreed in advance. The communities from which the mothers were selected and the characteristics of the study samples were described in detail in the report on the second phase (*2*). The groups studied in each of the countries, together with the number of human milk specimens provided for analysis, are specified in Table 2.

It was decided to study the composition of human milk at about three months after the birth of the baby. At this stage of lactation the milk is relatively mature and many of its constituents have reached fairly stable levels. Moreover, three months is the time at which many mothers start to wean their babies. After this age, therefore, the baby's intake of nutrients no longer depends exclusively on breast milk.

One of the important practical problems in this kind of research is that many of the elements of interest are present at such low levels that contamination of the samples by the use of impure or inadequately cleaned equipment can seriously affect the results. Specially prepared and cleaned collection vessels and specimen vials were therefore supplied to all collection centres. A special detergent (baby shampoo) containing low levels of trace elements was also supplied for washing the breast prior to the collection of the milk.

Details of the sample collection and reporting procedures are given in Annexes 1 and 2. For the analysis of the minor and trace elements by the reference analytical laboratories, samples of 20–30 ml of milk were requested. Some of the collection centres retained an additional