Vitamins and Minerals in Pregnancy and Lactation: An Introduction

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The determination of the nutritional requirements of the developing fetus and the newborn is a very complex problem, given that the optimum rate of growth has not been established with certainty. The model of fetal growth is growth in the intrauterine environment; the problem is more complex during extrauterine life. Maternal nutritional status at the time of conception, qualitative and quantitative intakes during pregnancy, and possible intervention programs during its course will influence intrauterine growth. Pregnancy itself and its far-reaching consequences, as well as interactions among nutrients, will also play a role.

A great number of enzymes regulating key metabolic pathways depend on the presence of trace elements and vitamins, and due to this, the effects of maternal nutritional deprivation could affect development of enzymes in fetal tissues. Through the studies of Widdowson and Spray (1) on 38 human fetuses and those of Apte and Iyengar (2) on the body composition of 41 fetuses of mothers from lower socioeconomic classes in India, we have some knowledge about the quantities of minerals in fetal tissues in the different stages of pregnancy. The rate of incorporation of different trace elements into fetal organs during pregnancy is very different for each organ, and in some aspects it follows a general law similar to that regulating the accretion of different compounds during specific periods of pregnancy.

With our co-worker, Fiol, we have studied the content of zinc, copper, and manganese of the whole cerebrum during the last trimester of intrauterine life and their rate of accumulation in the cells. For this purpose, the mineral and DNA content of the cell were compared. The study was carried out on 17 brains from newborns of gestational age ranging from 20 to 44 weeks who died during the first 24 hr of life without malformation. All mothers had normal gestation and normal nutritional status. Zinc, copper, and manganese values, expressed per total DNA, plotted versus gestational age, show a progressive increase with a parabolic profile at different levels for
each of the trace elements studied (Figs. 1-3). The curve for each trace element can be divided into two parts: the first from the 20th to the 30th week of gestation with homogenous values, and the second from the 30th week until the term of gestation, where the values increase rapidly. Zinc is the most abundant trace element and accumulates most rapidly in cerebrum, followed by copper and manganese. The accumulation of all three minerals follows a similar pattern in the cerebrum.

Hytten and Leitch (3) discussed whether or not the requirements of the fetus are covered by metabolic economy on behalf of the mother. Naismith (4) suggests that perhaps during pregnancy the requirements in energy, proteins, and all the other nutrients may be no more than those of nonpregnant women.

Some changes can be directly influenced by pregnancy itself; for example,
the high plasma concentration of 1,25-dihydroxycholecalciferol observed in the last trimester of pregnancy induces an increased uptake of calcium from the gut (5). The rise in plasma concentrations of vitamin A in the second half of pregnancy due to the high concentration of circulating retinol binding protein should be directly proportional to a release of retinol from the maternal liver, apparently induced by the rise of maternal estradiol (6,7). Our knowledge is incomplete concerning the metabolism of trace elements during pregnancy. Much of the existing information on minerals in pregnancy and lactation is of doubtful value because different dietary intakes of heterogeneous groups are represented; however, studies in animals suggest that even marginal deficiencies during prenatal life can have deleterious effects. It is evident that modern techniques for the measurement of trace elements in biological samples have made it easier to understand the role of trace elements and vitamins in the development of biological systems.

TRACE ELEMENTS AND THE CENTRAL NERVOUS SYSTEM

Deficiency as well as excess of some trace elements can have a deleterious effect on the development of the central nervous system (CNS) and its function (Table 1). Some of the consequences are known only in animals, both
FIG. 3. Manganese content of whole fetal cerebrum during the second half of intra-uterine life (mg/total DNA).

with regard to teratological and clinical aspects. This problem deserves further study in humans.

Iodine

Disorders resulting from severe iodine deficiency (8) have been estimated to affect more than 400 million people in Asia alone and several million more in Africa and Latin America. Motor performance is disturbed in children

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born from mothers living in iodine-deficient areas. Studies in Papua New Guinea (9) show that children born from mothers who had received iodine prophylaxis were significantly more rapid and precise in their response to tests of manual function than children from control mothers. The intelligence scores of children aged 3 to 7 years whose mothers had received iodized oil before pregnancy were better than those of the controls (10). Yet, how iodine affords protection for the fetus is uncertain (11).

**Cobalt**

According to observations in humans with cobalamin deficiency and in animals deprived of cobalamin, the role of cobalt for homeostasis of the nervous system has been established (12), but no precise data exist for newborns.

**Iron**

Iron deficiency can produce alterations in fine motor coordination and behavioral performance (13). In animals an association has been established between iron and dopaminergic neurons (14); however, an association between iron deficiency and neurological development in the newborn is not very probable, since Murray and Murray (15) in Nigeria demonstrated that mean iron concentrations in mother’s milk were the same in mothers with either depressed or full stores of iron at 2 weeks and at 6 months of lactation. Mixed feeding, as is the case of mother’s milk plus baby foods, can produce an inhibition of iron absorption from human milk (16).

**Zinc**

The effects of zinc deficiency in rat dams produced in the sucklings a decrease in total brain lipids, a diminished uptake of $[^3]H$thymidine by brain DNA and a decrease of $^{35}S$ uptake by brain proteins (17). Behavioral disturbances arise in the offspring of monkeys and rats from mothers with zinc deprivation during the last trimester of pregnancy (18).

**Chromium and Molybdenum**

Abnormal function of the central and peripheral nervous system has been described as a consequence of chromium deficiency during total parenteral nutrition (TPN) (19). Lethargy, night blindness, and coma have also been reported in molybdenum deficiency during TPN; however, data are lacking on clinical manifestations in the offspring of possible deficiencies in chro-
mium and molybdenum during pregnancy. Data are also lacking in general with regard to these deficiencies during lactation.

Copper

Maternal copper deficiency in ewes can produce neonatal enzootic ataxia in their lambs (21). Arrest of myelin formation has been associated with low brain cytochrome oxidase activity reported in copper-deficient animals (22). The role of copper in the developing brain has been well established by Smith (23) as well as by O'Dell and Prohaska (24). Copper deficiency is now well recognized in Menkes’ disease (25). On the other hand, an excess of zinc can disturb copper absorption, while copper accumulation is reported in Wilson’s disease.

Manganese

A tendency to convulsions has been reported in animals with manganese deficiency (26). Ataxia has been described in manganese-deficient chicks (27) and in rat pups (28), but no data are available concerning human newborns. An excess of manganese by inhalation has been associated with neurological disturbances but not in children (29).

Lead

Low IQ and a low level of attention have been described in children (30) who had not previously had lead poisoning but show increased lead values in deciduous teeth. Deficits in cognitive function associated with changes in the hair lead content have also been reported (31).

Mercury

A high content of inorganic mercury in water is conducive to high levels of methylmercury in fish. Fetuses of mothers who had eaten this contaminated fish sustained poisoning (32,33).

Aluminum

No data have been reported concerning possible aluminum toxicity in relation to mother’s diet during pregnancy or lactation. Aluminum toxicity, with high aluminum content in brain tissues in neonatal uremia, and the possible influence of the aluminum content of infant formula have been re-
ported (34). Dialysis encephalopathy syndrome has also been associated with aluminum intoxication (35), and aluminum accumulation has been reported in infants receiving TPN with aluminum-contaminated fluids (36).

Consequently, it is important to know the permissible limits of safety for concentrations of trace elements and vitamins during pregnancy and their essential levels in the diet during lactation.

INTERVENTION PROGRAMS IN PREGNANT WOMEN

Intervention programs in pregnant women receiving supplementary foods [Guatemala (37), Taiwan (38), Colombia (39), Gambia (40), New York (41), Thailand (42)] are usually designed to obtain information on the influence of supplementation, generally with regard to calories and protein, on the weight of the pregnant woman and the newborn. In the Oklahoma intervention program (43), a population of pregnant women at high risk was selected with the objective of approximating their diets to the recommended dietary allowance for pregnancy. The biochemical data obtained from this study showed that some nutrients increased their concentrations as a normal physiological consequence of pregnancy per se, whereas others such as zinc decreased.

Low plasma concentration of some nutrients in the pregnant woman may be the consequence of dilution owing to the increase in extracellular fluid or as a consequence of greater uptake by the placenta and the fetus (43). On the other hand, as has been demonstrated by Papoz et al. (44), women in general tend to change dietary habits during pregnancy, even when their nutritional status is normal; the study shows that there is a trend to increase the intake of calcium, vitamin C, vitamin B_{12}, carotene, and folic acid through high consumption of dairy products and vegetables.

Considerable evidence exists that periconceptional therapy with multivitamin preparations containing folate will protect mothers who have previously given birth to a child with neural tube defects and are planning a further pregnancy (45).

NUTRIENT INTERACTIONS

Nutritional deficiencies in vitamins or minerals can depend on specific conditions in different geographical areas. This applies to iodine, selenium, and chromium. Type of diet (e.g., a predominance of highly processed foods) consumed by pregnant and lactating women also influences the bioavailability of vitamins and trace elements. Bioavailability is influenced by non-nutrient components of the diet, such as phytates, oxalates, synthetic chelators, tanin, lignin, and fiber.

Possible interactions between essential and nonessential trace elements
or trace elements and vitamins also need to be considered. These antagonistic interactions, resulting in decreased bioavailability, occur at the intestinal level, interfering with absorption, or at the tissue level, disturbing utilization.

A mutual inhibitory effect exists between intestinal transport of zinc and folic acid (46). High levels of manganese interfere with iron metabolism (47), and iron supplementation has been shown to decrease manganese absorption in experimental animals (48). Zinc decreases iron bioavailability (49), excess copper decreases zinc absorption (50), and excess zinc can induce copper deficiency (51). Silver increases signs of copper deficiency (52), and there are interactions between cadmium and copper and zinc and iron (53). There are also correlations between dietary zinc deficiency and vitamin A metabolism in monkeys; vitamin A release and transport from the liver is related to plasma zinc concentrations (54). There are interconnections between pyridoxin and zinc metabolism; transitory zinc deficiency in the neonatal period has been related to megavitamin therapy of the mother during pregnancy (55). These interactions between nutrients can have clinical implications. For instance, zinc deficiency during pregnancy may have been induced by an antagonistic effect of prior supplements impairing zinc bioavailability (56).

MATERNAL DIET AND LACTATION

We shall briefly discuss some aspects of the influence of the mother’s diet and intake of trace elements and some vitamins on the content of these nutrients in breast milk (Table 2).

Iron

Infants exclusively breast-fed for 6 months do not show iron deficiency. One study (57) showed that 4% of such children had this deficiency at 9

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months, while another (58) confirms that breast-fed infants without iron supplements do not present iron deficiency for 5 months. A study in India (59) showed that women having a high incidence of anemia had high iron content in their breast milk, and it appears that a high maternal dietary iron intake does not have any effect on the content of this trace element in breast milk (60).

Copper

An increased copper intake is not reflected in breast milk. Even intravenous administration of copper produces no increase of the copper concentration in breast milk (61).

Chromium

Kumpulainen et al. (62) were unable to establish a correlation between dietary chromium intake and its content in human milk. Little information exists on chromium requirements in infants.

Fluorine

The fluorine content of breast milk shows similar values within the normal range, both for mothers drinking fluoridated water and those drinking water with low fluoride content (63).

Vitamin E

Khalid et al. (64) reported that 86% of Malaysian mothers were deficient in vitamin E when the serum vitamin E/serum total lipid ratio was used as an indicator; however, a study by the same team (65) suggests that human milk content of vitamin E is not dependent on maternal diet and that the stores of vitamin E probably ensure an adequate supply of vitamin E to the neonate during lactation.

Zinc

Daily supplementation of zinc to women during lactation has shown that, within a physiological range, milk concentrations of zinc are related to the intake (66).
Iodine

Women consuming iodized salt show higher iodine concentration in breast milk (67). Iodine supplements can also be given in the form of iodized oil by intramuscular injection, by mouth, or in iodized bread (68).

Manganese

The correlation between dietary intake of manganese and human milk content is constant (69). The content is thus influenced by variations in diet.

Selenium

Available information is contradictory. Levander et al. (70) found no correlation between the mother's dietary selenium and concentrations in breast milk, whereas Shearer and Hadjimarkos (71) did find a relationship. The values found by Robberecht et al. (72) in Belgium could relate to lower maternal intakes of selenium compared with other countries. In any case, there is wide variation between individual samples and evidence of geographical variance. A study in Japanese mothers (73) demonstrates a lack of significant correlation between selenium concentrations in breast milk, serum, or hair of lactating women.

Vitamin B\textsubscript{6}

Maternal supplements of vitamin B\textsubscript{6} are reflected in breast milk levels (74). It has been questioned whether or not vitamin B\textsubscript{6} supplementation during lactation could have an antiprolactinemic effect (75).

Riboflavin

Riboflavin intake or supplementation influences breast milk concentrations (76,77).

Vitamin C

Changes in vitamin C concentration in human milk could depend on quantitative intake. Various reports (78–80) showed increased vitamin C content in human milk when the intake increased; however, dietary intake of vitamin C in these women was low. Yet, other authors (81,82) found no increase in the levels of vitamin C in milk when lactating women received intakes of
vitamin C largely exceeding the recommended dietary allowance. The explanation would appear to be that mammary tissue becomes saturated, and a regulatory mechanism stops further increase of concentration in the milk. Plasma values of vitamin C decrease sharply during the first weeks of life in premature infants receiving pasteurized pooled human milk (83).

With the present tendency to prolong breast feeding, it is important to know what the changes will be, if any, of minerals and vitamins in breast milk during extended lactation. Data (84) indicate that zinc and calcium decrease, magnesium remains unchanged during 7 to 17 months, vitamin $B_6$ and C decrease, and folacin levels remain unchanged.

CONCLUSION

Although there is much data on trace elements and vitamins during pregnancy and lactation in humans and a great deal of information with regard to deficiencies in experimental animals, there is still little information on subclinical states of deficiency in mothers and on the influence of diets and supplements on breast milk composition. Possible antagonistic interactions need to be considered. This is a matter for research, not only in areas where overt primary deficiencies are prevalent, but also in developed countries, where the incidence of subclinical deficiencies could increase due to the consumption of highly purified manufactured diets and monotonous habits, induced by social pressure, instead of more natural and varied diets.

I trust that the data presented during the symposium on which this volume is based will contribute to shedding light on many of the questions that have so far remained unanswered.

REFERENCES


82. Byerley LO, Kirksey A. Effects of different levels of vitamin C intakes on the vitamin C
