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## **Nutrition in Pregnancy: three crucial periods for mothers and newborns**

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### **ABSTRACT**

It is well recognized that nutritional status during pregnancy is a key factor in modulating the characteristics of the environment within which the foetus originates and develops. Women's nutritional status just before conception and during early pregnancy may influence pregnancy outcomes by affecting critical developmental processes that begin early in pregnancy, as well as the availability of nutrients. Diet has also an important impact on the life of the newborn.

Recent studies showed that the impact of inadequate energy intake and micronutrients intake in pregnancy extends for decades, affecting both mothers and the offspring.

In this paper we review the main evidence on the role of diet in the preconceptional period, in pregnancy and in the post-partum period.

The article focuses on the need for the correct intake of micro nutrients based on the experience of different specialists who follow mothers and their babies (Gynecologist, Obstetrician, Pediatrician and Nutritionist).

**Keywords:** nutrition in pregnancy, micronutrients, supplementation, breastfeeding.

### **SOMMARIO**

È evidente che lo stato nutrizionale durante la gravidanza sia un fattore chiave nella modulazione delle caratteristiche dell'ambiente in cui il feto origina e si sviluppa.

Lo stato nutrizionale delle donne poco prima del concepimento e durante la gravidanza può influenzare l'esito della stessa condizionando i processi critici di sviluppo che iniziano nelle primissime fasi, così come la disponibilità di nutrienti.

La dieta ha anche un importante impatto sulla vita del neonato.

Studi recenti hanno dimostrato che l'impatto dell'insufficiente assunzione energetica e dell'insufficiente assunzione di micronutrienti in gravidanza si ripercuote per decenni, interessando sia madre che figlio.

In questo articolo vengono esaminate le principali prove sul ruolo della dieta nel periodo preconcezionale, in gravidanza e nel periodo post partum.

L'articolo si concentra sulla necessità della corretta assunzione di micronutrienti in base all'esperienza di diversi specialisti che seguono la madre e il bambino (Ginecologo, Ostetrico, Pediatra e Nutrizionista).

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## NUTRITION IN THE PRECONCEPTION PERIOD

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Nutrition in the preconception period is essential in order to improve fertility, promote the mother's ability to meet pregnancy and breastfeeding nutrition requirements. Moreover, nutrition is essential for the healthy development of an embryo, a foetus, an infant, and a child.

The FIGO recommendations, "Think Nutrition first", have recently listed the top six nutrients women need for future motherhood: folic acid, vitamin B12, iron, iodine, calcium and vitamin D. Moreover, the same recommendations emphasize the role of antioxidants in pregnancy outcomes<sup>(1)</sup>.

### *Folic Acid*

Folic acid lowers the risk of birth defects<sup>(2)</sup>: a recent review by Cochrane<sup>(3)</sup> confirmed that folic acid supplementation prevents the first and second occurrence of neural tube defects. For women of reproductive age, 400µg/day are recommended as supplements or through fortified foods.

Moreover, there is growing evidence that peripheral levels of folic acid are positively related with the success of assisted reproductive technology (ART) procedures. Two initial studies failed to show an association<sup>(4,5)</sup>, but subsequent large-scale studies showed a significant correlation<sup>(6-8)</sup>.

There is also evidence that the risk of miscarriage is lower in women with higher folic acid levels<sup>(9)</sup> and that inadequate maternal folate status is associated with low infant birthweight, preterm delivery and fetal growth retardation<sup>(10)</sup>.

### *Vitamin B 12*

Being naturally found in animal products, it is often difficult for vegetarians and vegans to get enough of this nutrient. Higher serum concentrations of folate and vitamin B12 before ART procedures were associated with higher live birth rates among the population exposed to folic acid fortification<sup>(7)</sup>.

Further vitamin B12 level supplementation in the preconception period was associated, with folic acid, with a reduced risk of malformations<sup>(11,12)</sup>.

### *Iron*

Iron is lost with menstruation bleeding and iron requirements are greater in pregnancy. It can be found in meat, liver, nuts, beans, dark leafy greens. Iron deficiency is quite common and is often associated with other nutritional deficiencies; it is the major cause of iron-deficiency anaemia.

A Cochrane review showed that daily oral iron supplementation in pregnant women significantly reduced the risk of low birthweight, and prevented maternal anaemia and iron deficiency in pregnancy<sup>(13)</sup>.

### *Iodine*

Iodine is essential for normal brain development. Moderate and severe foetal iodine deficiency results in substantial to serious developmental delay in children. For example, in a longitudinal study conducted in the UK, 8-year-old children were more likely to be in the lowest quartile of verbal IQ, if their mothers had mild iodine deficiency in early pregnancy, than children of mothers with normal iodine levels<sup>(14)</sup>.

### *Calcium*

Calcium is found in dairy products, canned fish bones, tofu, and beans. Calcium supplementation or foods fortified with calcium before or early in pregnancy and continued at least until mid-pregnancy showed to prevent pre-eclampsia and other hypertensive disorders, maternal morbidity and mortality, as well as to improve foetal and neonatal outcomes<sup>(15)</sup>. Further calcium supplementation in the second half of pregnancy reduces serious consequences of pre-eclampsia and is recommended by the World Health Organization (WHO) for women with low dietary calcium intake. Most data, however, are based on studies in which calcium supplementation was associated with antioxidants and other supplements.

### *Vitamin D*

Animal studies have shown that mice with 1-hydroxylase deficiency (the enzyme converting 25-hydroxy-vitamin-D [25(OH)D], the vitamin storage form, into the 1,25-di-hydroxy-vitamin-D biologically active form) are infertile and show uterine hypoplasia and the absence of corpus luteum<sup>(16)</sup>. In humans, it has been shown that the Vitamin D Receptor (VDR) is expressed in the ovary, endometrium and myometrium and that vitamin D deficiency promotes the development of fibroids and endometriosis<sup>(17)</sup>.

Although the role of vitamin D deficiency in human natural fertility has been poorly studied<sup>(18-20)</sup>, several observational data from IVF cycles are available. According to a recent meta-analysis, vitamin D deficiency was associated with decreased chances of a live birth after an IVF/ICSI procedure<sup>(21)</sup>. Noteworthy, vitamin D deficiency is quite common in the western world. In a study

conducted in Milan, the proportion of women scheduled for IVF with optimal serum levels of vitamin D was below 10% in winter and below 50% in summer<sup>(22)</sup>.

#### *Antioxidants*

The levels of vitamins such as vitamin A and vitamin E or Zinc can also affect pregnancy outcomes. The World Health Organization (WHO) recommends vitamin A supplementation during pregnancy in areas where there is endemic vitamin A deficiency, based on the expectation that supplementation can improve maternal and foetal outcomes (including mortality and morbidity) and prevent anaemia, infection and xerophthalmia<sup>(23)</sup>. The risk of pregnancy complications involving oxidative stress, such as pre-eclampsia, might be potentially reduced by antioxidant supplementation. Furthermore, local development of oxidative stress is believed to have significant adverse effects on the oocyte and the embryo, as well as on implantation (through DNA damage), membrane lipid peroxidation and protein oxidation.

Endometriosis, hydrosalpinx and polycystic ovary syndrome are some conditions that can be potentially caused by oxidative stress in sub-fertile women<sup>(24)</sup>. Antioxidants are expected to have a protective effect against the detrimental impact of oxygen free radicals. In particular, they can improve epithelial growth in blood vessels and in the endometrium<sup>(25)</sup>. Recently, antioxidant supplementation showed to improve success rates among women attending clinics for ART<sup>(26)</sup>.

#### *The need for supplementation*

It has always been thought that the Italian population is characterized by a high consumption of fruits and vegetables, and, consequently, by an adequate vitamin and other micronutrients intake, but this is not true.

For example, in a cross-sectional study conducted in Milan<sup>(27)</sup> on women observed in an infertility clinic, only 69% and 44% of women showed adequate levels of homocysteine and vitamin B12, respectively. Serum folate was appropriate in 78% of the study participants, but only a minority (12%) had a concentration of RBC folate considered as optimal for the prevention of fetal neural tube defects. Vitamin B12 levels were also found to be inadequate. Likewise, an analysis by Zappacosta et al.<sup>(28)</sup> conducted on a group of Italian blood donors found that, among women mainly of childbearing age who did not use folic acid supplements, only 30%, 23%, 25% and 15%

had adequate levels of serum folate, RBC folate, homocysteine and vitamin B12, respectively. With regard to the RBC folate threshold considered as optimal prior to conception (400ng/ml), none of the participants had adequate levels. Similar data also emerged in a study conducted on pregnant women<sup>(29)</sup>.

Iodine levels are also inadequate. In a study conducted in the urban area of Cassino in 2016-17, the majority of pregnant women and their foetuses was not protected from the detrimental consequences of iodine deficiency. Therefore, the identification of new strategies to increase the knowledge and awareness of the general population regarding the beneficial effects of iodine supplementation during pregnancy is highly required<sup>(30)</sup>.

All these data underlined the role of supplementation in women who are planning for a pregnancy.

## **NUTRITION DURING PREGNANCY – THE 1000 DAYS WINDOW**

### **H. Cena**

Scientific evidence confirms that the phenomena occurring in the early stages of life play a major role in fostering the development of chronic diseases later on in offspring, underlining the high relevance of “the maternal environment” impact on the life of the future child; therefore, it is universally acknowledged that nutritional status during pregnancy is a key factor in modulating the characteristics of the environment within which the foetus originates and develops. Women’s nutritional status just before conception and during early pregnancy may influence pregnancy outcomes by affecting critical developmental processes that begin early in pregnancy, as well as the availability of nutrients<sup>(31)</sup>.

Therefore, awareness of the relationship between nutrition and health in women of childbearing age should be raised, and this life period should become an opportunity for changes towards healthy lifestyles, providing optimum conditions for the present and future health of both the woman and her child. Since nutrition during the critical periods of preconception, conception, implantation, placentation and embryo- or organogenesis may influence pregnancy outcomes by altering both maternal and foetal metabolism, attention should be paid to nutrition also in the preconception period, in order to decrease adverse

pregnancy events such as pre-eclampsia and foetal growth outcomes. Recent studies showed that the impact of inadequate energy intake and micronutrients intake in pregnancy extends for decades, affecting both mothers and the offspring. Both over-nutrition and under-nutrition during pregnancy expose the newborn to the risk of impaired functional capacity in response to extra-uterine metabolic adaptation requests<sup>(32)</sup>.

Underweight women are exposed to greater risk of abortion in the first three months, and in case of malnourishment the foetus can be exposed to adaptive inability. Because malnutrition is a problem affecting not only developing countries but also developed countries, particular attention should be paid to women with a history of Eating Disorders, to adolescents, to those with a low SES (Socio Economic Status) and to those who had undergone a bariatric surgery procedure for morbid obesity<sup>(33)</sup>.

On the other hand, maternal obesity with high pre-pregnancy BMI or excessive weight increase during pregnancy, impacts pregnancy outcomes leading to the development of gestational hypertension, preeclampsia and gestational diabetes and induces both short-term effects on the foetus and the newborn, such as a twofold increased risk of delivering an infant with neural tube defects (NTDs)<sup>(34)</sup>, and long term ones affecting health during childhood, independently of other maternal comorbidities<sup>(35)</sup>.

Several studies described a positive association between elevated BMI and the risk of birth defects. Data on plasma concentration of folate in pregnant women with obesity showed values far below those recommended, regardless of the diet, while folate levels should increase before pregnancy to reduce neural tube defects, therefore folate status in women of childbearing age with obesity should be assessed to start personalised and more adequate supplementation before conception<sup>(36)</sup> and during pregnancy.

Moreover, recent studies demonstrated that maternal obesity during pregnancy is associated with alterations in the composition and diversity of the intestine microbial community<sup>(37)</sup>, influencing the microbial colonization and increasing the risk of metabolic diseases in the offspring<sup>(38)</sup>. This scenario may be particularly serious for obese women of childbearing age who may be subject to an increased risk of key nutrient deficiencies and inadequacies related to negative pregnancy outcomes<sup>(39)</sup>. Therefore, it is important to advise pregnant women to monitor their weight gain in pregnancy<sup>(40)</sup>.

During pregnancy, there is a higher daily energy demand due to increased expenditure and basal metabolic rate, caused by the placenta development, foetus growth, increased size of maternal organs, increased respiratory and cardiovascular work; so, the energy intake will need to be valued for each specific case on the basis of the actual daily energy expenditure, depending also on physical activities. Energy requirements should be met taking into account pre pregnancy BMI and the desirable weight gain according to the national reference values<sup>(41)</sup>. 2014 reference intake levels for energy intake for the Italian population (LARN) 2014 suggest additional requirements of 69 kcal/day for the first quarter, 266 kcal/day for the second and third 496 kcal/day trimester of pregnancy (for an overall total of 76,530 kcal). Values very similar to those established by EFSA (European Food Safety Authority): 70 kcal/day in the first trimester, 260 and 500 kcal/day in the second and third trimester, respectively<sup>(42)</sup>.

Food choices should be based on protein intake, dietary fats, vitamins and minerals. It is recommended to maintain an adequate intake of protein, whose requirements increase significantly from the second trimester, by eating fish, lean meats, eggs, dairy and legumes. An increased intake of proteins is required especially during the second and third trimester, and 21 grams per day are required for maternal tissues, placenta and foetal growth<sup>(41)</sup>.

During pregnancy, attention should also be paid to macronutrients, such as long chain n-3 polyunsaturated fatty acids (LC-PUFA), which play a critical role in foetal and infant growth and development. Maternal n-3 LC-PUFA supplementation may reduce the risk of early preterm birth (>34 weeks) and seems to be very promising for primary allergy prevention during childhood<sup>(43)</sup>. Since the LC-PUFA required by the foetus is supplied by preferential placental transfer of preformed LC-PUFA, rather than their precursor, it was hypothesized that additional maternal supply of LC-PUFA, especially DHA, during pregnancy may improve maternal and infant outcomes<sup>(43)</sup>. An association among n-3 fatty acids, serotonin transporter genotype, and postpartum depression was identified<sup>(44)</sup>, so diet quality, dietary intake of n-3 fatty acids, and overall nutritional status can impact the risk of postpartum depression<sup>(45)</sup>.

Although consumed in small quantities, vitamins and minerals play a key role, for human health; this role is even more important during pregnancy and breastfeeding, to the extent that

micronutrients requirement increases more than those of macronutrients. An inadequate intake of micronutrients, as well as poor nutritional diet variety, can have serious consequences for both the mother and the developing foetus.

Micronutrients such as iron, zinc, iodine and, as B-vitamins, vitamin A, folic acid and zinc influence oxidative pathways and methylation, and also affect embryogenesis, which occurs early in pregnancy and may be related to miscarriage and foetal malformations.

It is recommended to vary often the choices of fresh fruits and non-starchy vegetables (both yellow-orange and dark green leafy products), consume cereals (pasta, rice, barley, bread, etc.) on a daily basis, olive oil as a dressing and reduce consumption of salt preferring iodized one.

Furthermore, folic acid-containing supplements proved to reduce the incidence of first occurrence of NTDs, and are recommended globally before and in early pregnancy, while vitamin D supplementation during pregnancy reduces the frequency of baby low-birth-weight<sup>(39)</sup>. A meta-analysis of 31 observational studies and 4 RCTs conducted by Wolf et al.<sup>(46)</sup> evaluated the effect of multivitamin and mineral supplementation on pregnancy outcomes in developed countries, reporting a significant decreased risk of NTD recurrence, lower for gestational age infants, cardiovascular defects, urinary tract defects, and limb deficiencies.

Pregnant women also need to maintain an adequate level of hydration and avoid consumption of alcohol<sup>(47)</sup>. Alcohol consumption in pregnancy may increase the risk of miscarriage, intrauterine growth retardation, prematurity, low birth weight, and lead to neurodevelopment impairment later in life<sup>(45)</sup>. Beverages containing substances such as caffeine are to be consumed with caution too; moreover, both artificially sweetened and sugar-sweetened beverage have been recently reported to be associated with infant BMI<sup>(48)</sup>. Given the current epidemic of childhood obesity and widespread use of artificial sweeteners, dietary recommendations for pregnant women should also suggest what kind of beverages are to be limited or excluded during pregnancy. Pregnancy has been regarded as a maternal phase with requisite additional nutritional requirements and can prevent short and long term adverse events.

One of the most discussed issued is diet during pregnancy for food allergies prevention. Scientific evidence showed that there were no benefits from the restriction of food allergens in the diet

of pregnant (and breastfeeding) women from 'high risk' families with a family history of allergic diseases; in unselected samples ("normal risk families") the level of evidence is such that specific dietary restrictions for women during pregnancy cannot be recommended as a preventive strategy<sup>(49)</sup>. Since there is no consensus on the most effective strategy for the prevention of food allergies in newborns, we should consider the national guidelines<sup>(50)</sup> on this topic, which advocate moderate consumption of foods rich in pharmacologically vasoactive molecules or capable of releasing them, including fermented cheeses, shellfish, clams, cocoa/chocolate, that can trigger adverse reactions.

The composition and the diversity of the intestinal microbiota heritage are defendants in the multifactorial aetiology of allergic pandemic expansion, and the delivery method and the type of feeding are decisive for the postnatal bacterial colonization and the future composition of the gut microbiota. Nutrition during pregnancy plays a key role in the development, maintenance, and optimal functioning of immune cells and microbiota diversity. Nutrients, such as zinc and vitamin D and nutritional factors, such as pre- and probiotics, can influence the nature of an immune response and are important in ensuring appropriate functioning of the immune system<sup>(51)</sup>. Moreover, evidence is emerging regarding the role of fats and maternal n-3 LC-PUFA supplementation, which showed to reduce the risk of primary allergy during childhood<sup>(43)</sup>.

The aim of prenatal nutrition is to support a healthy uterine environment for optimal foetal development while supporting maternal health. The ideal prenatal diet should limit overconsumption for the mother and prevent under-nutrition for the foetus<sup>(52)</sup>.

With respect to the Italian population, the available data show that intakes of selected nutrients are often insufficient for both target population groups and pregnant and breastfeeding women<sup>(53)</sup>. This applies, in particular, to micronutrients like iron, iodine, calcium, folic acid, vitamin D as well as fats like DHA.

Therefore, besides a healthy lifestyle during pregnancy, which includes a balanced nutrition-focused diet, regular physical activity, food safety and hygiene practices and avoidance of harmful habits like smoking, alcohol or caffeine and/or sugar rich drinks consumption, supplementing vitamins, minerals and DHA are recommended, plus any additional vitamins or minerals if any deficiencies are detected. Supplements do not

replace a healthy diet, but ensure that a woman is receiving enough daily nutrients<sup>(54)</sup> and should always be considered, in particular, for women on exclusion diets, smokers, adolescents, for those with weight problems, multiple or close pregnancies, and previous unfavourable pregnancy outcomes, due to the increased risk of inadequate supply of nutrients to support maternal and infant health<sup>(36,43,53,54)</sup>.

## POSTPARTUM NUTRITION

### D. Corvino

Often, the well-being of pregnant women, including nutritional aspects, is neglected immediately after childbirth when biological, hormonal and lifestyle changes require adequate support. In particular, meeting the increased energy and nutrient requirements, protecting the mother's health and promoting a regular growth of the newborn are objectives to be pursued in line with a healthy lifestyle.

Stress and physical and mental fatigue, associated with feelings of inadequacy and a lack of time for personal care and the preparation of proper meals often induce new mothers to neglect their own diet, which translates into frugal meals, long hours of fasting, unhealthy food choices, consumption of ready meals or junk-food, poor nutritional quality foods, high fat and high sugar meals with no adequate amounts of micronutrients recommended for the well-being of every woman and her baby after delivery. Often new mothers, in an attempt to return to their pre-pregnancy fitness, follow miraculous restrictive, unbalanced diets poor in vitamins and minerals that do nothing but increase the level of stress.

As it happens with pregnancy, in fact, the nutritional needs for new mothers change not only in terms of energy and macronutrients, but also and above all in terms of micronutrients. For some of them – such as calcium, phosphorus, magnesium – the requirement remains as high as in pregnancy<sup>(47)</sup> given the important function for the growth and formation of bones, which consist mainly of these components, their involvement in energy and metabolic processes, as well as in neuro-muscular transmission. Vitamins are also essential micronutrients; in particular, among fat-soluble vitamins, vitamin D, which is essential for calcium absorption, and among water-soluble vitamins, vitamin B12, which is essential for preventing and/or correcting anaemia,

often associated with the postpartum period and for its “neurotrophic” action that mitigates susceptibility to psycho-physical stress. Being contained exclusively in foods of animal origin, vitamin B12 must necessarily be integrated into vegetarian and vegan women, often not well informed of the real risks induced by prolonged vitamin B12 deficiency, not only for them but also for children. With regard to anaemia prevention, for new mothers, vitamin C requirements also increase, since it favours the absorption of iron and of vitamin B6, whose role in the degradation of homocysteine makes it an essential vitamin for the prevention of cardiovascular diseases (venous thrombosis) and of depression symptoms often characterising the postpartum period<sup>(55)</sup>.

Due to its important antioxidant and photo-protective function, as well as its role in the prevention of retinopathies in premature infants, lutein is also extremely important<sup>(56)</sup>.

Contained in green leafy vegetables, lutein bioavailability is also high in broccoli, potatoes, asparagus, and breast milk is also characterized by high concentrations of lutein. So, during breastfeeding, taking this beta carotenoid is as important as taking calcium (by intake of water with a high content), iodine (using little and iodized salt), zinc, copper, selenium, vitamin A, B vitamins, vitamin C and an adequate quantity of proteins<sup>(47)</sup>. During this period, it is recommended to reduce the consumption of foods, such as onion, garlic, asparagus, spices, and so on, that can alter the taste of milk and affect breastfeeding. Maintaining an adequate level of hydration during pregnancy, and even more during breastfeeding with water, tea, or rather caffeine free tea, herbal teas or other unsweetened drinks, is crucial, not only when feeling thirsty<sup>(41)</sup>. In fact, milk production is metabolically expensive in terms of water consumption, because the latter is the major component of breast milk in which all other nutrients are dissolved. The LARN, the Reference Levels of Nutrient and Energy Intake for the Italian Population, recommend a surplus of about 700ml of water compared to consumption during pregnancy (2000ml/day). Its function on fluid homeostasis, transport of useful substances and the elimination of catabolites, as well as on maintenance of body temperature, just when the hormonal structure changes significantly, make it an essential component even in the postpartum period. Alcohol consumption, on the other hand, should always be avoided in the postpartum period, as well as during pregnancy: 15 minutes after taking alcohol, the alcohol level in the

foetus is similar to that of the mother. During breastfeeding, alcohol is quickly and easily distributed from the blood to milk and then to the baby. Alcohol can also reduce the production of breast milk<sup>(47,57,58)</sup>.

A proper nutrition, the right information and an integration of the micronutrients required for healthy and balanced maternal nutrition, allow to meet the nutrition requirements for new mothers in a delicate and demanding period, that is after childbirth, whether the baby is breastfed or not, because the assumption that a mother who eats well is a healthy mother and will have a baby who will eat well in the future is still valid.

## NUTRITIONAL NEEDS DURING BREASTFEEDING

### A. Lops

There is new important knowledge about nutritional needs during the breastfeeding period. 2014 LARN (Reference Levels of Nutrient and Energy Intake for the Italian Population)<sup>(41)</sup> provide new reference values for energy and nutrients, also considering some "delicate" periods in life, such as breastfeeding.

During breastfeeding, as well as during pregnancy, an increase in maternal energy needs must be expected, necessary for the production of milk, whose caloric density is determined primarily by the fat content.

The additional energy requirement for breastfeeding women is related to the quantity of milk produced. 2 to 3 weeks after childbirth, a nursing mother generally provides the infant with 500 to 600ml of milk every day, which can then increase up to 850ml. Although very variable from woman to woman, the synthesis of milk can be approximately 810ml per day, on average, an amount that decreases progressively during weaning. To ensure adequate milk production, nursing mothers need to increase their daily intake of calories by 500 kcal/day. An insufficient energy intake during breastfeeding mainly leads to a reduction in the volume of the milk produced, which changes only minimally in terms of composition.

Although found in diets in reduced amounts, micronutrients (vitamins and minerals) play a basic role for body functions, becoming even more important during pregnancy and breastfeeding. Micronutrient requirements, indeed, increase more than those of macronutrients<sup>(53)</sup>.

### Iron

As postpartum bleeding increases the probability of maternal anemia, even in industrialized countries almost 50% of women need iron supplementation at this stage.

The secretion of iron in milk is rather limited, therefore WHO (World Health Organization) and FAO (Food and Agriculture Organization of the United Nations) support a decrease in iron intake during breastfeeding, compared to other fertile stages, to compensate for amenorrhea.

In the absence of menstruation, women should take 11mg/day to be increased to 18mg/day in case of return of menstruation.

### Iodine

During breastfeeding, iodine requirements increase as a result of changes in maternal metabolism, also to promote milk secretion.

The intake recommended during breastfeeding is 200µg/day, so as to guarantee a iodine content in the milk of about 100 to 150µg/100mL.

### Calcium

Calcium maternal requirements are met with a daily intake of about 1000mg. The amount of calcium secreted on a daily basis in breast milk is quite variable (150 to 300mg/day) and depends mainly on the mobilization of calcium from bone deposits. Despite the concurrent reduction of urinary calcium secretion, this results in a temporary loss of bone density during breastfeeding<sup>(59)</sup>.

Some studies showed that calcium secretion in milk is substantially independent of its dietary intake and of supplementation. Therefore, the recommended intake during breastfeeding is not different from that of the healthy adult female population (1.0g/day). However, women with dietary calcium intakes lower than 300mg/day and adolescents, with high basal requirements (1.2g/day according to the RDA) are at risk of deficiency also during breastfeeding.

### Vitamin D

Even during breastfeeding, the risk of vitamin D deficiency is mainly for ethnic groups with hyper-pigmented skin or with low exposure to sunlight, given the influence of sunlight exposure on vitamin D metabolism. Vitamin D food intake is usually sufficient, but may be inadequate, particularly in situations of greater needs and in countries where food sources are reduced. An intake of 15µg/day (600IU/day) is necessary to meet the requirements of this vitamin during

breastfeeding. These levels can be increased up to 1000-2000IU/day in case of vitamin deficiency risk factors for the duration of breastfeeding.

However, breast milk amounts of vitamin D (<80 IU/l) are not enough to prevent vitamin D deficiency in the first year of life<sup>(60)</sup>. Maternal supplementation is not considered sufficient for the needs of the newborn, who must therefore be directly supplemented.

#### *Folate*

Folate concentrations in breast milk progressively increase from colostrum to mature milk, to much higher levels than plasma. The absence of a correlation between maternal and milk status suggests an active role of the mammary gland in the transport and regulation of folate secretion, only marginally influenced by dietary intake<sup>(61)</sup>.

During breastfeeding, folate intake should be increased by 25%, up to 500µg/day<sup>(62)</sup>.

The concentration in breast milk of many other vitamins (thiamin, riboflavin, vitamin B6, vitamin B12, vitamin A) depends on maternal vitamin levels: a maternal vitamin deficiency usually corresponds to human milk deficiency.

#### *DHA*

Although it is not a micronutrient, special attention should also be paid to DHA.

DHA is the major polyunsaturated fatty acid contained in the human brain and retinal rods, it plays major roles in the psychomotor neurodevelopment in the first months of life, when it is supplied at high amounts by breastmilk.

The benefits of DHA for the foetus and for the infant are supported by an extensive literature, which confirms the importance of appropriate

omega-3 intake for maternal health, for the composition of breastmilk, and for overall infant health<sup>(63)</sup>. According to EFSA and the Italian RDA, DHA requirements increase to 100 to 200mg per day during pregnancy and breastfeeding.

There is some evidence that approximately 80% of the population (also in Italy) does not ingest the daily amount of EPA and DHA recommended by international guidelines (250 to 500mg daily).

The consumption of two servings of fish per week allows to get the adequate DHA content in breastmilk. The EFSA report concludes that consumption of more than 3 to 4 servings of fish/week does not provide any additional benefit. In order to balance adequate amounts of EPA and DHA and lower the risk of environmental contaminants, smallest fish such as sardines, anchovies and mackerel should be preferred<sup>(64)</sup>.

## CONCLUSION

Maternal good nutrition during the preconceptional period and pregnancy and good nutrition of children in the earliest years it are essential for lifelong health. They provide the building blocks for brain and immune system development and healthy growth<sup>(59)</sup>.

From the review it is clear that the supplementation of micronutrients is necessary in all three stages of pregnancy. Supplementation is not intended as a substitute for proper nutrition but as an aid to maintain adequate nutritional intake. Women and parents need and deserve practical and trustworthy information on nutrition. Gynecologists, Obstetricians, Pediatricians and Nutritionists play an important role in providing this information.

## REFERENCES

1) Hanson MA, Bardsley A, De-Regil LM, Moore SE, Oken E, Poston L, Ma RC, McAuliffe FM, Maleta K, Purandare CN, Yajnik CS, Rushwan H, Morris JL. **The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think**

**Nutrition First"**. Int J Gynaecol Obstet. 2015 Oct;131 Suppl 4:S213-53. doi: 10.1016/S0020-7292(15)30034-5  
2) Czeizel AE, Dudás I, Vereczkey A, Bánhidy F. **Folate deficiency and folic acid supplementation: the prevention of neural-tube defects and congenital heart defects.** Nutrients. 2013 Nov 21;5(11):4760-75)

- 3) De-Regil LM, Pena-Rosas JP, Fernandez-Gaxiola AC, et al. **Effects and safety of periconceptional oral folate supplementation for preventing birth defects.** *Cochrane Database Syst Rev.* 2015;12:CD007950
- 4) Haggarty P, McCallum H, McBain H, Andrews K, Duthie S, McNeill G, Templeton A, Haites N, Campbell D, Bhattacharya S. **Effect of B vitamins and genetics on success of in-vitro fertilisation: prospective cohort study.** *Lancet.* 2006 May 6;367(9521):1513-9
- 5) Boxmeer JC, Macklon NS, Lindemans J, Beckers NG, Eijkemans MJ, Laven JS, Steegers EA. **Steegers-Theunissen RPIVF outcomes are associated with biomarkers of the homocysteine pathway in monofollicular fluid.** *Hum Reprod.* 2009 May;24(5):1059-66. doi: 10.1093/humrep/dep009. Epub 2009 Feb 15
- 6) Gaskins AJ, Afeiche MC, Wright DL, et al. **Dietary folate and reproductive success among women undergoing assisted reproduction.** *Obstet Gynecol.* 2014;124:801-9
- 7) Gaskins AJ, Chiu YH, Williams PL, et al. (EARTH Study Team). **Association between serum folate and vitamin B-12 and outcomes of assisted reproductive technologies.** *Am J Clin Nutr.* 2015 Oct;102(4):943-950
- 8) Paffoni A, Castiglioni M, Ferrari S et al. **Homocysteine pathway and in vitro fertilization outcome.** *Reprod Toxicol.* 2017;76:12-16
- 9) Gaskins AJ, Rich-Edwards JW, Hauser R, et al. **Maternal prepregnancy folate intake and risk of spontaneous abortion and stillbirth.** *Obstet Gynecol.* 2014;124:23-31
- 10) Fekete K, Berti C, Trovato M, et al. **Effect of folate intake on health outcomes in pregnancy: a systematic review and metaanalysis on birth weight, placental weight and length of gestation.** *Nutr J.* 2012;11:75
- 11) Botto LD, Olney RS, Erickson JD. **Vitamin supplements and the risk for congenital anomalies other than neural tube defects.** *Am J Med Genet C Semin Med Genet.* 2004;125:12-21
- 12) Sutton M, Mills JL, Molloy AM, Troendle JF, Brody LC, Conley M, Mc Donnell R, Scott JM, Kirke PN. **Maternal folate, vitamin B12 and homocysteine levels in pregnancies affected by congenital malformations other than neural tube defects.** *Birth Defects Res A Clin Mol Teratol.* 2011 Jul;91(7):610-5. doi: 10.1002/bdra.20817. Epub 2011 May 17
- 13) Pena-Rosas JP, De-Regil LM, Dowswell T, et al. **Daily oral iron supplementation during pregnancy.** *Cochrane Database Syst Rev.* 2012;12:CD004736
- 14) Bath SC, Steer CD, Golding J, et al. **Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC).** *Lancet* 2013;382:331-7
- 15) Hofmeyr GJ, Manyame S. **Calcium supplementation commencing before or early in pregnancy, or food fortification with calcium, for preventing hypertensive disorders of pregnancy.** *Cochrane Database Syst Rev.* 2017 Sep 26;9:CD011192
- 16) Panda DK, Miao D, Tremblay ML, et al. **Targeted ablation of the 25-hydroxyvitamin D 1alpha-hydroxylase enzyme: evidence for skeletal, reproductive, and immune dysfunction.** *Proc Natl Acad Sci USA.* 2001;98:7498-503
- 17) Buggio L, Roncella E, Somigliana E, Vercellini P. **Vitamin D and benign gynecological diseases: a critical analysis of the current evidence.** *Gynecol Endocrinol.* 2016;32(4):259-63
- 18) Somigliana E, Paffoni A, Lattuada D, et al. **Serum Levels of 25-Hydroxyvitamin D and Time to Natural Pregnancy.** *Gynecol Obstet Invest.* 2016;81:468-71
- 19) Fung JL, Hartman TJ, Schleicher RL, Goldman MB. **Association of vitamin D intake and serum levels with fertility: results from the Lifestyle and Fertility Study.** *Fertil Steril.* 2017;108:302-311
- 20) Wise LA, Wesselink AK, Mikkelsen EM, et al. **Dairy intake and fecundability in 2 preconception cohort studies.** *Am J Clin Nutr.* 2017;105:100-110
- 21) Zhao J, Huang X, Xu B, Yan Y, Zhang Q, Li Y. **Whether vitamin D was associated with clinical outcome after IVF/ICSI: a systematic review and meta-analysis.** *Reprod Biol Endocrinol.* 2018 Feb 9;16(1):13. doi: 10.1186/s12958-018-0324-3
- 22) Pagliardini L, Vigano P, Molgora M, et al. **High Prevalence of Vitamin D Deficiency in Infertile Women Referring for Assisted Reproduction.** *Nutrients.* 2015 Dec 2;7(12):9972-84
- 23) World Health Organization. **Global prevalence of vitamin A deficiency in populations at risk 1995–2005.** Geneva: WHO; 2009
- 24) Ruder EH, Hartman TJ, Blumberg J, et al. **Oxidative stress and antioxidants: exposure and impact on female fertility.** *Hum Reprod Update.* 2008;14:345–357
- 25) Takasaki A, Tamura H, Miwa I, et al. **Endometrial growth and uterine blood flow: a pilot study for improving endometrial thickness in the patients with a thin endometrium.** *Fertil Steril.* 2010;93:1851–1858
- 26) Buhling KJ, Grajecki D. **The effect of micronutrient supplements on female fertility.** *Curr Opin Obstet Gynecol.* 2013;25:173–180
- 27) La Vecchia I, Paffoni A, Castiglioni M et al. **Folate, homocysteine and selected vitamins and minerals status in infertile women.** *Eur J Contracept Reprod Health Care.* 2017 Feb;22(1):70-75
- 28) Zappacosta B, Persichilli S, Iacoviello L, Di Castelnuovo A, Graziano M, Gervasoni J, Leoncini E, Cimino G, Mastroiacovo P. **Folate, vitamin B12 and homocysteine status in an Italian blood donor population.** *Nutr Metab Cardiovasc Dis.* 2013 May;23(5):473-80
- 29) Parazzini F, Chiaffarino F, Ricci E, Improta L, Monni G. **Homocysteine, red cell, and plasma folate concentrations and birth weight in Italian women: results from a prospective study.** *J Matern Fetal Neonatal Med.* 2011 Mar;24(3):427-31. doi: 10.3109/14767058.2010.501127. Epub 2010 Jul 20
- 30) Tuccilli C, Baldini E, Truppa E, D'Auria B, De Quattro D, Cacciola G, Aceti T, Cirillo G, Faiola A, Indigeno P, D'Aliesio L, Gazzellone F, Bononi M, D'Armiento E, Carbotta G, Pironi D, Catania A, Sorrenti S, Ulisse S. **Iodine deficiency in pregnancy: Still a health issue for the women of Cassino city, Italy.** *Nutrition.* 2018 Jun;50:60-65. doi: 10.1016/j.nut.2017.11.007. Epub 2017

Nov 27

31) **Paediatric and Perinatal Epidemiology**, 2012, 26 (Suppl. 1), 285-301

32) Myatt L. **Placental adaptative responses and fetal programming** - J Physiol 2006; 572: 25-30

33) Pelizzo G, Calcaterra V, Fusillo M, Nakib G, Ierullo AM, Alfei A, Spinillo A, Stronati M, Cena H. **Malnutrition in pregnancy following bariatric surgery: three clinical cases of fetal neural defects**. Nutr J. 2014 Jun 14;13:59. doi: 10.1186/1475-2891-13-59

34) Scialli AR. **Public Affairs Committee of the Teratology Society: Teratology public affairs committee position paper: maternal obesity and pregnancy**, Birth Defects Res A Clin Mol Teratol 76:73, 2006

35) Mitanchez D, Chavatte-Palmer P. **Review shows that maternal obesity induces serious adverse neonatal effects and is associated with childhood obesity in their offspring**. Acta Paediatr. 2018 Feb 8. doi: 10.1111/apa.14269

36) Maffoni S, De Giuseppe R, Stanford FC, Cena H. **Folate status in women of childbearing age with obesity: a review**. Nutr Res Rev. 2017 Dec;30(2):265-271. doi: 10.1017/S0954422417000142

37) Zhou L, Xiao X. **The role of gut microbiota in the effects of maternal obesity during pregnancy on offspring metabolism**. Biosci Rep. 2018 Apr 13;38(2). pii: BSR20171234. doi: 10.1042/BSR20171234

38) Houttu N, Mokkalá K, Laitinen K. **Overweight and obesity status in pregnant women are related to intestinal microbiota and serum metabolic and inflammatory profiles**. Clin Nutr. 2017 Dec 27. pii: S0261-5614(17)31433-4. doi: 10.1016/j.clnu.2017.12.013

39) Blumberg JB, Cena H, Barr SI, Biesalski HK, Dagach RU, Delaney B, Frei B, Moreno González ML, Hwalla N, Lategan-Potgieter R, McNulty H, van der Pols JC, Winichagoon P, Li D. **The Use of Multivitamin/Multimineral Supplements: A Modified Delphi Consensus Panel Report**. Clin Ther. 2018 Apr;40(4):640-657. doi:10.1016/j.clinthera.2018.02.014

40) Cena H, Toselli A, Bagnara A, Turconi G. **Assessment of weight gain during pregnancy: an Italian practical approach**. Minerva Ginecol. 2009 Apr;61(2):97-107

41) Società Italiana di Nutrizione Umana: **Raccomandazioni secondo la IV rev. dei livelli di assunzione di riferimento di nutrienti ed energia per la popolazione italiana**, LARN 2014

42) <http://www.sinu.it/public/pdf/NFI---Documento-alimentazione-materna-it.pdf>

43) De Giuseppe R, Roggi C, Cena H. **n-3 LC-PUFA supplementation: effects on infant and maternal outcomes**. Eur J Nutr. 2014 Aug;53(5):1147-54. doi: 10.1007/s00394-014-0660-9

44) Shapiro GD, Fraser WD, Séguin JR. **Emerging risk factors for postpartum depression: Serotonin transporter genotype and omega-3 fatty acid status**. Can J Psychiatry, 57 (11) (2012), pp. 704-712

45) Procter SB, Campbell CG. **Position of the Academy of Nutrition and Dietetics: Nutrition and Lifestyle for a Healthy Pregnancy Outcome**, Journal of the Academy of Nutrition and Dietetics, Volume 114, Issue 7, 2014, Pages 1099-1103, ISSN 2212-2672, <https://doi.org/10.1016/j.jand.2014.05.005>

46) Wolf HT, Hegaard HK, Huusom LD, Pinborg AB. **Multivitamin use and adverse birth outcomes in high-income countries: a systematic review and meta-analysis**. Am J Obstet Gynecol, 217 (2017), p. 404 e1-404. e30

47) **Linee guida per una sana alimentazione italiana**, INRAN 2003

48) Meghan B. Azad, PhD; Atul K. Sharma, MSc, MD; Russell J. de Souza, RD, ScD; Vernon W. Dolinsky, PhD; Allan B. Becker, MD; Piuskumar J. Mandhane, MD; Stuart E. Turvey, MBBS, DPhil; Padmaja Subbarao, MD; Diana L. Lefebvre, PhD; Malcolm R. Sears, MB; **Association Between Artificially Sweetened Beverage Consumption During Pregnancy and Infant Body Mass Index** for the Canadian Healthy Infant Longitudinal Development Study Investigators. JAMA Pediatr. doi:10.1001/jamapediatrics.2016.0301 Published online May 9, 2016

49) Da Silva D, Geromi M, Halcken S, Host A Panesar SS, Muraro A, Werfel T, Hoffmann-Sommergruber K et al. On behalf of the EAACI Food Allergy and Anaphylaxis Guidelines Group. **Primary Prevention of food allergy in children and adults: systematic review**. Allergy 2014

50) [http://www.salute.gov.it/portale/salute/p1\\_5.jsp?lingua=italiano&id=110&area=Vivi\\_sano](http://www.salute.gov.it/portale/salute/p1_5.jsp?lingua=italiano&id=110&area=Vivi_sano)

51) Mazzocchi A, Venter C, Maslin K, Agostoni C. **The Role of Nutritional Aspects in Food Allergy: Prevention and Management**. Nutrients. 2017;9(8):850. doi:10.3390/nu9080850

52) Shapira N. **Prenatal nutrition: A critical window of opportunity for mother and child**, Womens Health, 4 (6) (2008), pp. 639-656

53) Marangoni F, Cetin I, Verduci E, Canzone G, Giovannini M, Scollo P, Corsello G, Poli A. **Maternal diet and nutrient requirements in pregnancy and breastfeeding**. An Italian Consensus Document, Nutrients 2016, 8, 629; doi:10.3390/nu8100629

54) <http://americanpregnancy.org/pregnancy-health/nutrients-vitamins-pregnancy>

55) Zaric BL, Obradovic M, Bajic V, Haidara MA, Jovanovic M, Isenovic ER, **Homocysteine and Hyperhomocysteinaemia**. Curr Med Chem 2018 Mar 12 doi:10.2174/092986732566618031310594. PubMed PMID

56) Cena H, Castellazzi AM, Pietri A, Roggi C, Turconi G. **Lutein concentration in human milk during early lactation and its relation ship with dietary lutein intake**. Public Health Nutr. 2009 Oct; 12 (10): 1878-84. doi:10.1017/S1368980009004807. Epub 2009 Feb 16. PubMed PMID: 19216808

57) Scafato E, Gandin C, Patussi V e il gruppo di lavoro IPIB. **L'alcol e l'assistenza sanitaria primaria. Linee guida cliniche per l'identificazione e l'intervento breve**. ISS, Osservatorio Nazionale CNESPS- OMS; testo originale [www.phepa.net/units/phepa/html/en/dir361/doc13210.html](http://www.phepa.net/units/phepa/html/en/dir361/doc13210.html)

58) **Global Recommendations on Physical Activity for Health**. WHO 2010

59) Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L, Torloni MR. **Calcium supplementation during pregnancy for preventing hypertensive disorders**

**and related problems.** Cochrane Database Syst Rev. 2014;6:CD001059  
60) Wagner CL, Greer FR, American Academy of Pediatrics Section on Breastfeeding, et al. **Prevention of rickets and vitamin D deficiency in infants, children, and adolescents.** Pediatrics 2008; 122(5): 1142-52  
61) O'Connor DL, Green T, Picciano MF. **Maternal folate status and lactation.** J Mammary Gland Biol Neoplasia. 1997;2(3):279-89  
62) EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2014. **Scientific Opinion on**

**Dietary Reference Values for folate.** EFSA Journal 2014;12(11):3893, 59 pp  
63) Mennitti LV, Oliveira JL, Morais CA, Estadella D, Oyama LM, OllerdoNascimento CM, Pisani LP. **Type of fatty acids in maternal diets during pregnancy and/or lactation and metabolic consequences of the offspring.** J. Nutr. Biochem. 2015, 26, 99-111  
64) European Food Safety Authority (EFSA). **Statement on the benefits of fish/seafood consumption compared to the risks of methylmercury in fish/seafood.** EFSA Journal 2015; 13:3982