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Selenium in Pregnant Women: Mini Review

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Abstract

Selenium (Se) is a trace element extremely important for proper development and growth of the organism. The concentration of Se in blood components of women in early stages of pregnancy varies widely from one country to another and depends, largely, on the amount of daily dietary selenium intake. Se intake of 1 μg/kg body weight, i.e., 60 μg-70 μg per day, is recommended for adults. Dietary Se intake in the world is highly differentiated, from 30 μg-50 μg in most European countries to more than 100 μg in the USA, Canada and Japan. Many authors have shown that in pregnant women who have a relatively low level of Se in the body, during pregnancy the concentration of the element decreases. In contrast, in women with a high concentration of Se in the body, the concentration usually is unchanged. A pregnant woman transmits the element from her body to the developing fetus. This element progressively accumulates in the organs of the growing fetus. Breast milk concentration reflects maternal selenium intake and increases in response to selenium intake. Since the deficiency of Se in humans can lead to various complications (spontaneous abortion, preeclampsia, low birth weight), a number of authors recommend that women planning to become pregnant or being at an early stage of pregnancy and have low blood level of Se should have this element administered.

Keywords: Selenium supplementation; Pregnancy; Plasma; Women

Introduction

The concentration of selenium (Se) in the blood of women during pregnancy varies from country to country. According to most authors as pregnancy progresses, the level of the element progressively decreases, while others have not observed any differences between the beginning and the end of pregnancy. The results may depend on the content of selenium in the body of pregnant women. In the present paper I would like to review the results of those studies.

The daily dietary intake of Se depends on many factors, including: the amount of selenium in the soil of a given country, type of food consumed, place of residence (town/village) and many others [1-3]. Humans consume Se in the form of selenocysteine (Sec; animal products) or selenomethionine (SeMet; plant products). In plasma Se is incorporated or bound to certain proteins. The main form of Se in mammalian tissues is selenocysteine (Sec), the 21st amino acid [3]. Se in this form is essential for the synthesis of selenoproteins and is found in the active center of a number of selenoprotein enzymes. It should be mentioned that in humans, three proteins containing Se are present in plasma, viz. glutathione peroxidase (GSH-Px) and selenoprotein P (SePP); the third protein is albumin, which does not incorporate Sec, but binds Se in the form of SeMet. Butler and Whanger [4] calculated that during pregnancy Se is incorporated into the plasma GSH-Px (13%-17%), SePP (50%-60%) and bound to albumins (23%-32%).

Among the 25 known selenoproteins an important enzymatic activity is played by GSH-Pxs and SePP [5-7]. Both proteins are involved in the antioxidant defense of the body. Their level depends on the concentration of Se [8,9]. Plasma SePP concentration falls in selenium deficiency [10]. Xia et al. [9] demonstrated that in subjects with low concentration of Se in plasma, with increasing level of the element, concentrations of both proteins increased. This has been confirmed by Rayman et al. [8] in pregnant women: SePP concentrations in plasma at the 35th week of gestation were 3.00 μg/mL and 5.30 μg/mL in the placebo group and in the group supplemented with Se, respectively (Figure 1) [8].

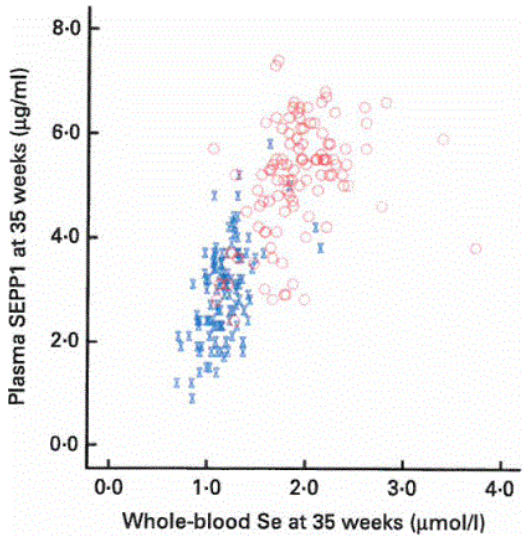

Figure 1: Selenoprotein P (SePP) vs. whole blood selenium concentration at 35 weeks of pregnancy: x, placebo; o, selenium. Adapted with permission from Rayman et al. [8].

SePP contains up to 10 selenocysteines, therefore its proposed main function is the transport and delivery of Se to tissues [5,6]. Human

SePP is an accessible index of Se nutritional status that appears to be more useful than plasma GSH-Px activity of Se concentration [5,10].

Soil and thus agricultural products of most European countries are relatively low in Se [11-13], hence the concentration of Se in the blood is low [14,15]. This is the reason why most publications, especially those referring to European countries, showed much lower concentrations of Se in pregnant women's plasma [16-22]. Similarly, a decrease of Se concentration has also been observed in amniotic fluid [23].

In 1980, the Food and Nutrition Board of the National Research Council proposed a safe and adequate range of selenium intake for adults to be 50 μg/day to 200 μg/day [24]. Later, based on determinations of plasma GHS-Px activities in humans who were administered increasing doses of selenium, the recommended selenium intake was calculated as 70 μg/day and 55 μg/day for adult men and women, respectively [25].

In the majority of European countries Se intake among residents is relatively low [14,26,27] and ranges from about 30 μg/day to 70 μg/day [28]. Selenium intake in the United Kingdom fell from a mean of 60 μg/day in 1991 to a minimum of 30 μg/day to 40 μg/day in 1995–2000; in 2010 the mean intake was 48 μg/day-58 μg/day [29].

In Finland (a country where the soil contains the lowest amount of Se in Europe) until 1984 the daily selenium intake was below 40 μg/day [30]. After enriching the soil with fertilizers containing sodium selenite, in the late 1980s the element content of agricultural products and in foodstuffs increased several times, and the estimated selenium intake in 1986 increased to 92 μg/day and in the next few years to 110 μg/day. As a result of this treatment, the concentration of Se in the serum increased from about 60 μg/L (before the year 1980) to 120 μg/L in 1990s [31].

Fish are a rich source of selenium. People who eat fish products consume a large amount of selenium. It has been shown [32] that in Italy the average daily Se intake were 90 μg if the diet included at least one weekly meal based on fish products. This value dropped to 60 μg/day if the diet did not involve fish consumption. The majority of Se in Japanese diets comes from fish and shellfish (57%) [2]. The daily intake of fish and shellfish with high Se levels has not changed markedly over the past few decades, going from 76 g-96 g. The daily intake levels of Se for 1957 to 1989 averaged 129 μg/day (66 μg–206 μg). In some US states (South Dakota and Wyoming; high selenium areas) average selenium values in the late 1980s were as follows: dietary intake, 174 μg/day (2.33 μg/kg body weight); serum, 166 μg/L [33]. Men and women had similar mean values of Se in blood components and toenails. Se intake was strongly correlated with Se concentrations in serum (r=0.63), whole blood (r=0.62) and toenails (r=0.59); (all values, P<0.01).

The level of Se in serum/plasma in adult European population ranges from about 40 μg/day to 84 μg/L [34]. In the Polish population the concentration of Se in blood plasma has been relatively low-about 50 μg/day-55 μg/L and the calculated daily dietary Se intake was about 30 μg/day-40 μg/day [27,35,36]. In German adults it was determined that Se concentration in serum is 75 μg/L and the daily dietary intake in men is 47 μg and that in women - 38 μg, corresponding to 0.67 μg/kg body weight per day for both men and women [37]. It has been shown that Se values of 100 μg/L in serum are believed to be required for saturation of the Se-enzyme-plasma glutathione peroxidase activity, an indicator of selenium repletion [38,39].

Se concentration in the plasma depends on its content in the body of the examined subject. Se levels in the body differ significantly between countries. This is related to the Se level in the soil of the given country and thus to the level of Se in the daily dietary intake [40].

The total content of Se in the body of adults in Poland has been calculated to about 5.2 mg [36], in German male subjects of 70 kg - approximately 6.6 mg [41], in women in New Zealand: 3.0 mg to 6.1 mg [42], while in the USA (Vermont [43]) is more than twice as high and amounts to 14.6 mg (13 mg-20 mg) [44].

A person with low content of Se in the body has lower concentration of this element in the plasma. A pregnant woman transfers Se through the placenta to the developing fetus.

Many authors believe that the Se requirements of pregnant women are increased as a result of selenium transport to the fetus [45]. The fetus accumulates Se especially at the end of pregnancy by storing it in the liver [46]. It is very likely that the concentration of Se in the plasma of pregnant women depends on the amount of the element in the organism. In women with low Se content in the body its concentration in plasma decreases with the progress of pregnancy. This is very often observed in pregnant women in Europe: Se concentration in the plasma in the third trimester and at delivery was significantly decreased when compared with the beginning of pregnancy [19,21,22,38,45-48]. Some examples are shown in Table 1.

Authors	Healthy controls	First trimester	Second trimester	Third trimester	Statistics (P)
Behne and Wolters [19]*	88 ± 11	89 ± 1	83 ± 10	74 ± 12a	<0.001
Mihailovic et al. [47]¶	68	63	50a	51a	<0.001
Anttila et al. [16]¶		59	63	51a	<0.05
Zachara et al. [22]¶	55.4 ± 10.9	53.4 ± 8.0	42.3 ± 9.4a	34.2 ± 9.1a	<0.001
Winnefeld et al. [48]¶		80.5 ± 11.05	60.8 ± 11.8a	56.1 ± 11.8a	<0.01

Table 1: Selenium concentration in plasma/serum in women during pregnancy with relatively low baseline selenium level. The primary data from Mihailoviac and Anttila could not be obtained; therefore interpretation of the results about concentration of Se is based on a graph in the publication. *, μg/kg plasma; ¶, μg/L plasma or serum; astatistically different from controls and/or 1st trimester of pregnancy.

There are very few publications reporting relatively high Se levels in the plasma of European women in early pregnancy, levels that were maintained throughout pregnancy. In Finland, after enriching in 1984 the soil with selenium, the concentration of the element throughout the entire pregnancy was 106 ± 15 μg/L, 107 ± 14 μg/L and 108 ± 15 μg/L at the first, second and third period, respectively [49].

A reduction in maternal Se concentration during pregnancy can lead to various disorders such as miscarriage, premature birth, preeclampsia, pregnancy induced hypertension, low birth weight, retinopathy of prematurity and some others [50-54]. Barrington et al. [52] showed that in the first trimester in women whose pregnancy ended with a miscarriage, Se serum concentration was significantly

lower compared with the first trimester of healthy pregnant women (54.7 μg/L vs. 65.3 μg/L, respectively; P<0.01). Se concentrations in both groups were significantly lower compared with non-pregnant women controls (81.1 μg/L; P<0.001). Identical values were obtained in comparable groups of Turkish women [55]. Al-Kunani et al. [56] have shown, however, that the serum concentration of Se in women who miscarried was the same as in the group of non-pregnant women (112 μg/L and 111 μg/L), but it was significantly lower in the hair (0.14 μg/g vs. 0.34 μg/g; P<0.001). The authors believe that because the difference was seen in hair samples but not in serum samples, selenium may not represent a simple nutritional deficiency. The authors' suggestion that other factors may contribute to miscarriage seems to be justified because Nicoll et al. [57] did not show any differences in Se concentration in the plasma of women with recurrent miscarriage and in pregnant women who did not have such disorders. Zachara et al. [58] have also shown that the selenium concentrations in whole blood and plasma of women following abortion were the same as in viable pregnancy, but were significantly lower compared with controls.

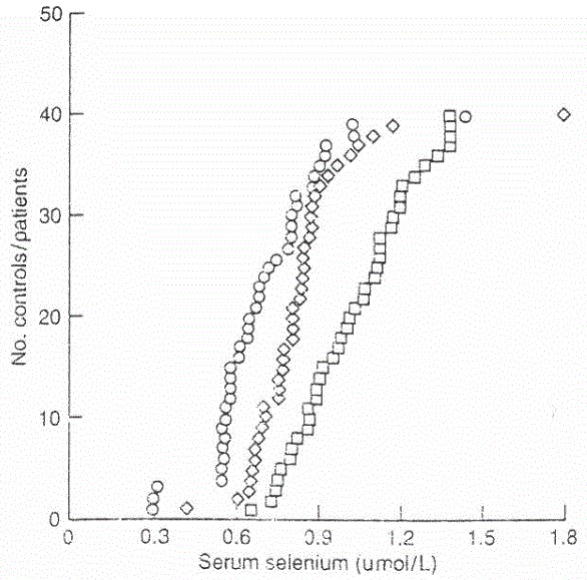

Figure 2: Distribution of serum selenium in controls (☒), viable pregnancies (◊) and first trimester miscarriage (○). Adapted from Barrington et al. [52].

Figure 2 shows the concentration of Se in the serum of healthy non-pregnant women (81.1 ± 16.0 μg/L), viable pregnancies (65.3 ± 16.3 μg/L; P<0.0001 vs. non-pregnant women) and miscarriages in the first trimester (54.7 ± 16.7 μg/L; P<0.0054 vs. normal pregnant controls) [52]. Rayman et al. [54] have shown that in the United Kingdom low selenium level in pregnant women is associated with the occurrence of the preeclampsia disease. The median level toenail Se in the preeclampsia women was significantly lower (0.56 mg/kg) than in the control women (0.62 mg/kg; P<0.001).

In a recent study, Rayman et al. [8] investigated the effect of selenium supplementation on the risk of pre-eclampsia in pregnant women (from 12 to 14 weeks of gestation until delivery) with low whole blood selenium concentration. In a double-blind, placebo-controlled trial, 230 pregnant women from the UK was randomized to selenium (60 μg/day, as selenium-enriched yeast) or placebo, from 12-14 weeks of gestation until delivery. The baseline Se concentration in whole blood (a longer term measure of Se status than plasma Se) was the same in both groups (1.32/1.31 μmol/L=104.2/103.4 μg/L). Between 12-35 weeks of gestation, whole blood selenium concentration increased significantly in the selenium-supplemented group (from 103.4 μg/L to 147.6 μg/L; P<0.0001) but decreased significantly in the placebo group (from 104.2 μg/L to 91.6 μg/L (P<0.0001). At 35 weeks, significantly higher concentrations of plasma SePP were observed in the selenium-supplemented group (5.3 μg/mL) than in the placebo group (3.0 μg/mL; P<0.0001).

Rayman et al. [8] assessed the number of pre-eclampsia and pregnancy-induced hypertension (PIH). There were eleven cases of pre-eclampsia (eight in the placebo group and three in the Se-treated group), and nine cases of PIH (six in the placebo group and three in Se-treated group). These data indicate that administration of Se reduces the risk of pre-eclampsia in pregnant women. However, as expected, the effect of Se treatment on the incidence of either outcome failed to reach significance. In another study, Rayman et al. [59] studied pregnant women with parameters similar to those mentioned [8]. The authors believe that because women in the UK have low Se concentration in blood and Se supplementation significantly reduced pre-eclampsia in PIH, women who are planning to become pregnant, or are at the beginning of their pregnancy should be supplemented with selenium. In this respect not only Rayman et al. [8] believe that in order to prevent the above mentioned complications, to pregnant women with low concentration of Se in blood should have this element administered. Suboptimal Se status is assumed when plasma/serum Se level is below 50 μg/L [60,61].

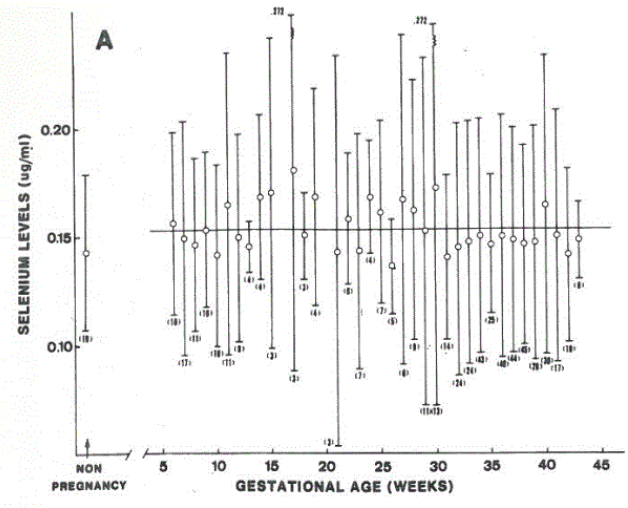

Figure 3: Distribution of serum selenium levels in pregnant women from southeastern South Dakota. Horizontal line represents the mean of mean values of all gestational ages. Adapted from Kundu et al. [69].

Opinions as to the amount of Se administration to pregnant women are not consistent. Neve [46] suggests that pregnant women with low Se concentrations in the plasma, irrespective of the diet, should be administered from 25 μg to 50 μg Se per day during pregnancy and lactation. Thomson and Robinson [62] believe that the dietary intake of Se in pregnancy should vary from 30 μg in New Zealand (the lowest

Se region in the world) up to 100 μg/day in some parts of the United States.

High and sometimes even higher concentrations of Se in pregnant compared with non-pregnant women are extremely rare and concern residents living in selenium-rich regions such as the United States [63-66], Venezuela [67], Japan [68] and probably some other regions. According to King [63] and Swanson et al. [64] in the United States the daily Se intake by pregnant women throughout the entire period of pregnancy exceeded 150 μg. Population studies assessing the relationship between Se intake during pregnancy and health outcomes in other countries are scarce [50].

In women with high concentration of Se in plasma (above 100 μg/L), changes in its concentration during pregnancy differ significantly in comparison to pregnant women having low concentration of selenium. Kundu et al. [69] determined Se concentration in human pregnancy at various gestational ages in 410 women living in South Dakota, USA (soil and thus agricultural products are rich in selenium). Se concentration in the serum of non-pregnant women was slightly lower than in pregnant women in the 6th week of pregnancy (just below and about 150 μg/L, respectively). No change in the levels of selenium was observed during pregnancy. This means that pregnancy had no effect on the maternal Se serum level (Figure 3). Swanson et al. [64] measured the amount of Se in pregnant women and showed that the amount of Se consumed by non-pregnant (150 μg daily) and pregnant women (154 μg and 158 μg per day compared to the beginning and end of pregnancy) is nearly the same. The results of studies by several authors are presented in Table 2.

Authors	Healthy controls	First trimester	Second trimester	Third trimester	Statistics (P)
Kundu et al. [69]*	-	151	151	151	NS
Sekine et al. [68]*	123.0 ± 12.1	140.2 ± 12.4	135.8 ± 7.5	143.3 ± 6.1	NS
Butler and Whanger [71]¶	-	0.14 ± 0.03	0.17 ± 0.02[a]	0.18 ± 0.02[a]	<0.0001
Swanson et al. [33]*	126	118	-	116	NS
Nwagha et al. [70]*	109.0 ± 14.2	107.4 ± 15.8	82.9 ± 17.4[a]	79.7 ± 18.9[a]	<0.0001 vs. ctr and 1st trim

Table 2: Selenium concentration in plasma/serum in women during pregnancy with relatively high baseline selenium level. The primary data from Kundu et al. [69] could not be obtained; interpretation of the results about concentration of Se level is based on a graph in the publication. [a]Statistical values were calculated only in the group of pregnant women without the group of non-pregnant women.

King [63] studied selenium intake as well as its absorption and secretion with urine and faeces in California women in the early and late stages of pregnancy and in non-pregnant controls, and found that Se intake did not differ significantly between non-pregnant women, and the two periods of pregnancy and amounted to 150 μg/day, 154 μg/day and 158 μg/day, respectively. The percentage of absorption did not differ significantly in the three groups and ranged from 78 to 84. The pregnant women excreted less urinary selenium than did the non-pregnant women, and the conservation of selenium was more pronounced in late than in early pregnancy. Thus, pregnant women seem to meet their selenium needs for pregnancy by decreasing urinary losses.

Interesting results have been obtained by Butler and Whanger who examined pregnant women in Corvallis, Oregon, USA. In one study, the authors showed that in plasma of pregnant women, who were supplied with placebo, a decline of Se concentration occurred during pregnancy [71]. In another study, the same authors [4] examined 63 women, ranging from early stages of pregnancy (2-3 months) until delivery. The analysis of dietary intakes of Se revealed an average of 70 μg/day (range of 35 μg/day to 120 μg/day). Because the primary data from this study could not be obtained, interpretation of the results about Se concentration in plasma is based on a graph found in the publication and the table. The initial concentration of Se in the plasma of all pregnant women was about 142 μg/g-146 μg/g. The authors showed that in women who received placebo (selenium free) there was an increase in the concentration of Se throughout pregnancy, while in women receiving 100 μg or 200 μg Se/day (yeast Se) plasma Se levels increased very significantly up to about seven-eight months and then declined just before the delivery in both the placebo group and in the group supplied with 100 μg Se (Figure 4). There was a greater increase of Se in plasma of women taking 200 μg Se daily. According to the authors Se requirement during pregnancy does not appear to be greater than 70 μg/day.

The above values for changes in the concentration of Se in plasma in women during pregnancy differ somewhat in different stages of pregnancy. Many authors believe that the Se requirements of pregnant women are increased as a result of selenium transport to the fetus via the placenta [27]. It has also been shown [56,57] that the administration of Se to nursing mothers leads to an increase in the concentration of this element in the mother's blood and in the blood of breast-fed infants as well as in the milk of lactating women. As a result, infants consume more selenium, an amount appropriate for their age [57].

Not only in plasma, but also in the whole blood and erythrocytes Se concentration in pregnant women with a relatively high concentration of the element in the body, is significantly ($P<0.05$) higher compared with the concentration in non-pregnant women. The GSH-Px activity in red blood cells of full-term pregnant women was also significantly higher than in non-pregnant women ($P<0.01$) [52].

Studies other than the ones presented by the above-mentioned authors who showed no changes in the concentration of Se in the blood of women with relatively high concentrations of the element during pregnancy [33,68,69,71] are those of Nwagha et al. [70]. They have shown that despite the high concentration of Se in the plasma of women in early pregnancy, during the progress of pregnancy a reduction of the concentration occurred. In women in southeastern Nigeria Se concentration in blood serum, during the first trimester of pregnancy (<14 weeks) is high and similar to that in non-pregnant women. Se concentration in both groups (first trimester of pregnancy and non-pregnant women) was relatively high compared to the results of many other authors and was 1.36 μmol/L (=107.4 μg/L) and 1.38 μmol/L (=109.0 μg/L), respectively. In the second (<14-27 weeks) and third trimester (<27 weeks) of pregnancy this concentration significantly decreased to 1.05 μmol/L (=82.9 μg/L), and 1.01 μmol/L (=79.7 μg/L, respectively; $P<0.0001$). What is significant about this

study is that the studied population belonged to the middle class, consisted mainly of urban population who may have a varied diet including bread from imported wheat (mainly from USA which is reach in selenium). The estimated daily Se intake in pregnant women was 100 µg (first trimester) and 110 µg (non-pregnant women). In the second and third trimester Se intake increased slightly to 110 µg and 120 µg per day, respectively. All the women were supplemented with routine iron and folic acid only.

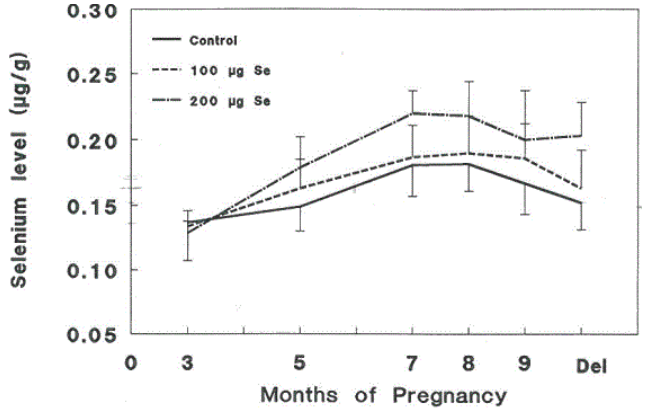

Figure 4: Plasma selenium levels in pregnant women taking no additional Se or 100 µg and 200 µg Se daily. The values at each point are means ± SD, as indicated by the bars. Adapted from Butler and Whanger [4] with permission.

The decrease in the concentration of plasma Se in pregnant women with low plasma concentration and the unchanged or even increased concentration during pregnancy and in women with a high concentration of this element in the plasma is not easy to explain. Some authors [12] believe that women with low blood Se concentration have a severely depleted Se depot in the body, and the growing fetus - by drawing on it - decreases it even further. When blood - and thus also the body - Se levels are higher, the depot is probably sufficiently large, so that fetus accumulation of Se does not affect maternal blood Se levels.

The results presented by Nwagah et al. [70] on relatively high intake of selenium and a fairly high plasma Se levels in pregnant and non-pregnant women differ fundamentally from the results reported by Kundu et al. [69], Butler and Whanger et al. [71] and Sekine [68]. Results are interesting but further studies are required to permit a more precise interpretation of this problem.

Conclusion

During pregnancy the concentration of Se in the blood of pregnant women, especially those with a relatively low level of this element in the body, decreases due to it transfer to the developing fetus. In women with a high Se level in the blood during pregnancy the concentration of the element is largely kept stable. Some authors believe that women with low Se level who are planning pregnancy or are in the initial period of pregnancy should be supplemented with this element.

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