Pregnancy, thyroid and selenium

- Selenium is important for the thyroid, especially for pregnant women
- Selenium deficiency impairs the thyroid
- Selenium deficiency increases the prevalence of thyroiditis (inflammation of the thyroid)
- Selenium requirements in patients with chronic thyroiditis are increased
- Selenium and iodine are an essential duo for the thyroid

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What is most important in short

Selenium and the thyroid gland	High selenium requirements of the thyroid
	Selenoproteins regulate thyroid metabolism
	Selenoproteins protect thyroid tissue
Pregnancy, thyroid and selenium	Increased risk of thyroid disorders during pregnancy
	Thyroid disorders have far-reaching consequences for mother and child
	Negative impact of hypothyroidism on the brain development of the baby
	Risk screening identified only 20 percent of those affected
	Selenium reduces the risk of postpartal thyroiditis in TPO antibody positive pregnant women
	Selenium reduces the TPO antibody titer postpartal
	Selenium inhibits the postpartum deterioration of thyroiditis
	Selenium deficiency increases the risk of pre-eclampsia
	Selenium supplementation reduces the risk of pre-eclampsia
	Selenium deficiency increases the risk of premature birth
	Selenium supplementation protects from postpartum depression
	Lower selenium status during pregnancy negatively influences the development of the baby

Selenium dosage in pregnancy

+ 300 µg selenium per day

Simultaneous use with L-Thyroxine possible

Summary of product characteristics for selenase®

selenase® pharmaceuticals

selenase® 100 µg peroral
Oral solution. 100 µg selenium per drinking ampoule

selenase® 300 Mikrogramm Tabletten
Tablets. 300 µg selenium per tablet

Active substance: Sodium selenite pentahydrate. Prescription only

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Selenium and the thyroid

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Selenium deficiency impairs the thyroid
Selenium deficiency increases the prevalence of thyroiditis
Chronic thyroiditis creates increased selenium requirements
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Selenium and iodine: an essential duo for the thyroid

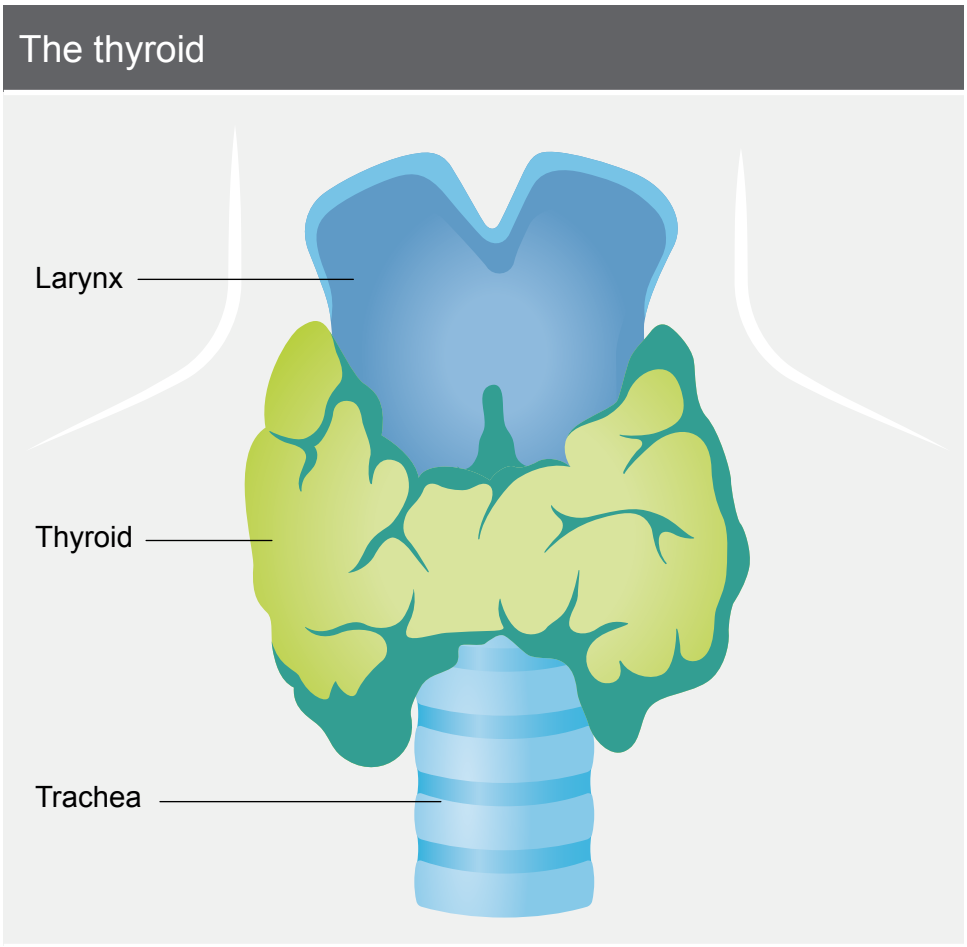


Fig. 1

The thyroid

The thyroid is a small butterfly-shaped organ that produces hormones. It lies below the larynx and in front of the trachea. In addition, four lentil-sized parathyroid glands are located on the back side of the thyroid. The medical term for the thyroid is thyroidea and is derived from Latin. Many terms associated with the thyroid are derived from this word, such as thyroiditis (inflammation of the thyroid).

The thyroid is not large (7 – 11 cm wide, approx. 4 – 5 cm high and weighing 18 – 25 grams), but its functions have an effect on the entire body *(Fig. 2)*. The thyroid produces and stores important hormones, which it releases into the blood at need. The so-called thyroid hormone activates many important metabolic processes in the body that put people in a state of readiness to take action. Thus the thyroid has a great impact on vitality and well-being.

Functions of the thyroid

Brain & psyche
- Growth of children
- Required for normal brain development
- Excitability of cells ↑
- Energy consumption ↑
- metabolic rate ↑

Heart
- Heart rate ↑
- Blood pressure ↑
- Vascular dilatation ↑

Muscles
- Protein consumption ↑
- Energy production ↑
- Tensioning and relaxation speed ↑

Stomach & intestines
- Intestinal motility ↑
- Sugar, fat and connective tissue metabolism ↑

Skin
- Activity of sweat and sebaceous glands ↑

Bones
- Preservation of bone substance

Fig. 2

Selenium is essential for the thyroid

Selenium is an essential trace element. The thyroid is an organ that is rich in selenium.[1,2] The high selenium requirements of the thyroid are due to so-called selenoproteins, which are indispensible for the thyroid. As the name already suggests, selenoproteins contain selenium. In contrast to other proteins, which bind trace elements such as copper (e. g. superoxide dismutase) or zinc (e. g. zink finger proteins), the genetic code was expanded for selenium. The genetic code codes a 21st amino acid, selenocysteine. Meanwhile, 25 different selenoprotein genes are known.

Selenoproteins activate thyroid hormones and protect the thyroid from oxidative stress

Numerous selenoproteins are essential for the thyroid. They activate the thyroid hormone[1,3] and protect the thyroid from oxidative stress.[1,4] On the one hand this involves deiodinase, which converts the inactive thyroid hormone thyroxine (T4) into its active form triiodothyronine (T3). At the same time, the selenoproteins are responsible for converting T3 into diiodothyronine (T2) and thus inactivating the thyroid hormons again. Deiodinases therefore play an important role in the regulation of the thyroid metabolism.

Additional essential selenoproteins are the glutathione peroxidases, which reduce the oxidative hydrogen peroxide (H_2O_2), which is formed at the generation of thyroid hormones, to water, thereby disarm it *(Fig. 3)*.

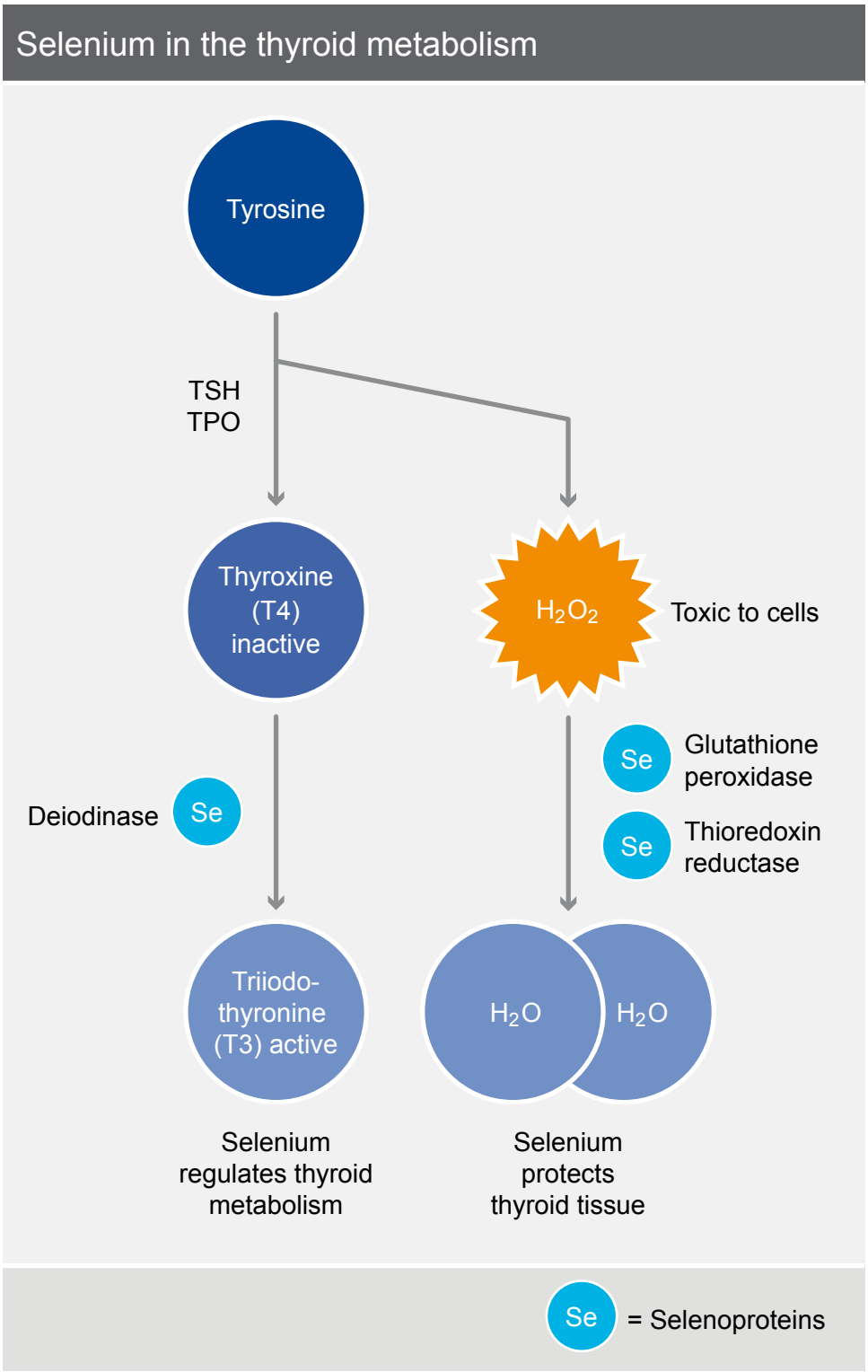

Selenium in the thyroid metabolism
Tyrosine
TSH
TPO
Thyroxine (T4) inactive
H_2O_2
Toxic to cells
Deiodinase
Se
Se
Glutathione peroxidase
Se
Thioredoxin reductase
Triiodo-thyronine (T3) active
H_2O
H_2O
Selenium regulates thyroid metabolism
Selenium protects thyroid tissue
Se
= Selenoproteins

Fig. 3

Selenium deficiency impairs the thyroid

Insufficient intake of selenium has a direct impact on the body's production of selenoproteins. There is a hierarchy of selenoproteins. If selenium is not sufficiently available to the body, certain selenoproteins that are essential for the body are preferred. The production of nonessential selenoproteins is reduced by up to 90 percent during periods of selenium deficiency. Both the glutathione peroxidase 1, the most important and most frequent glutathione peroxidase in the thyroid, as well as deiodinase are nonessential selenoproteins. The impact of a selenium deficiency therefore affects the selenoproteins that are essential for the thyroid the most.

If the thyroid has insufficient available deiodinase, the conversion of inactive T4 in active T3 is disturbed.[5] The relationship of T4 to T3 in the serum increases, which can result in thyroid disorders.

The reduced production of glutathione peroxidase results in increased oxidative stress, since hydrogen peroxide and organic peroxides are no longer sufficiently degraded.[6] The oxidative stress damages the thyroid tissue. At the same time this also promotes thyroid inflammation and disorders *(Fig. 4)*.[6]

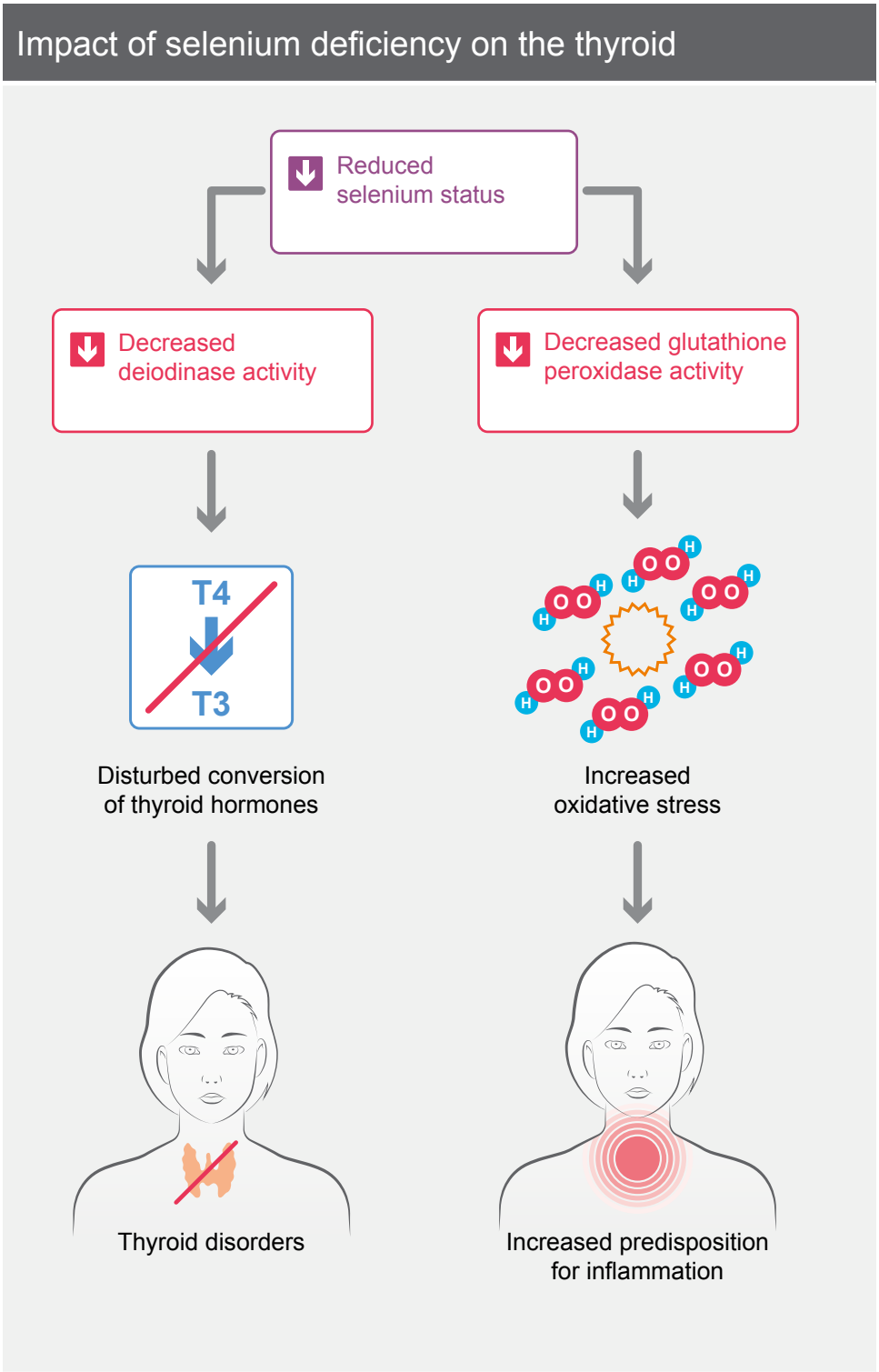

Impact of selenium deficiency on the thyroid
Reduced selenium status
Decreased deiodinase activity
Decreased glutathione peroxidase activity
T4
T3
Disturbed conversion of thyroid hormones
Increased oxidative stress
Thyroid disorders
Increased predisposition for inflammation

Fig. 4

Thyroiditis

An inflammation of the thyroid tissue is called a thyroiditis. Most frequently, thyroiditis is caused by an autoimmune disease. But also bacteria, viruses, injuries to the thyroid or radiotherapy can cause the thyroid to become inflamed.

Frequently types of thyroiditis are distinguished by the disease course: acute, subacute and chronic thyroiditis. The discussion below is exclusively concerned with chronic thyroiditis.

The best known form is Hashimoto autoimmune thyroiditis, a hypothyroidism. An example for hyperthyroidism is the autoimmune Graves' disease. Furthermore, a distinction is made between clinical and subclinical thyroiditis. If there are changed thyroid parameters (e.g. low-echo ultrasound, increased TPO antibody levels), but the thyroid functions normally, one speaks of subclinical thyroiditis. Thyroid dysfunction is called clinical thyroiditis.

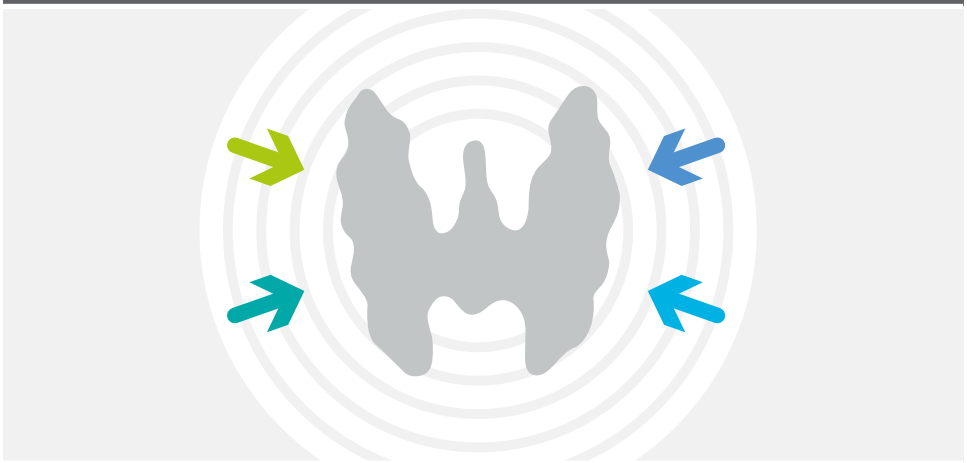
Causes of chronic thyroiditis

The mechanisms of pathogenesis have so far not been completely clarified. Experts assume that genetic predisposition and certain endogenous or exogenous factors the development of chronic thyroiditis promote *(Fig. 5)*.[7,8] Meanwhile, various gene variants are known which mediate a genetic disposition for the disorder.[8] A genetic disposition, however, is not alone decisive. The outbreak of the disease is dependent on additional factors.

Possible triggers of chronic thyroiditis are:[7]

- Selenium deficiency
- Changes in the hormon metabolism (for example, in puberty, after pregnancy or menopause)
- Viral infections
- Stress
- Intake of high-dose iodine (for example, iodized contrast medium)
- Immune stimulating medications (like interferon and interleukin)

Causes of chronic thyroiditis



Genetic factors	
Endogenous factors	• Sex hormones (pregnancy, puberty, menopause)
Selenium deficiency	• Oxidative stress • Tissue destruction
Environmental factors	• Iodide (highly dosed) • Virus infections • Stress • Immune stimulating medications

Duntas LH. Ann Endocrinol (Paris). 2011 Apr;72(2):108-13. doi: 10.1016/j.ando.2011.03.019. Environmental factors and thyroid autoimmunity.

Fig. 5

Selenium and iodine – an essential duo for the thyroid

Iodine is essential for the production of thyroid hormones. An iodine deficiency can therefore lead to thyroiditis. Thanks to comprehensive iodination primarily of table salt, iodine deficiency has been significantly reduced world-wide. On an average, Germany is located in the lower middle range of iodine intake recommended by WHO. [9] Germany is consequently no longer an iodine-deficient area, but is also not yet sufficiently supplied.

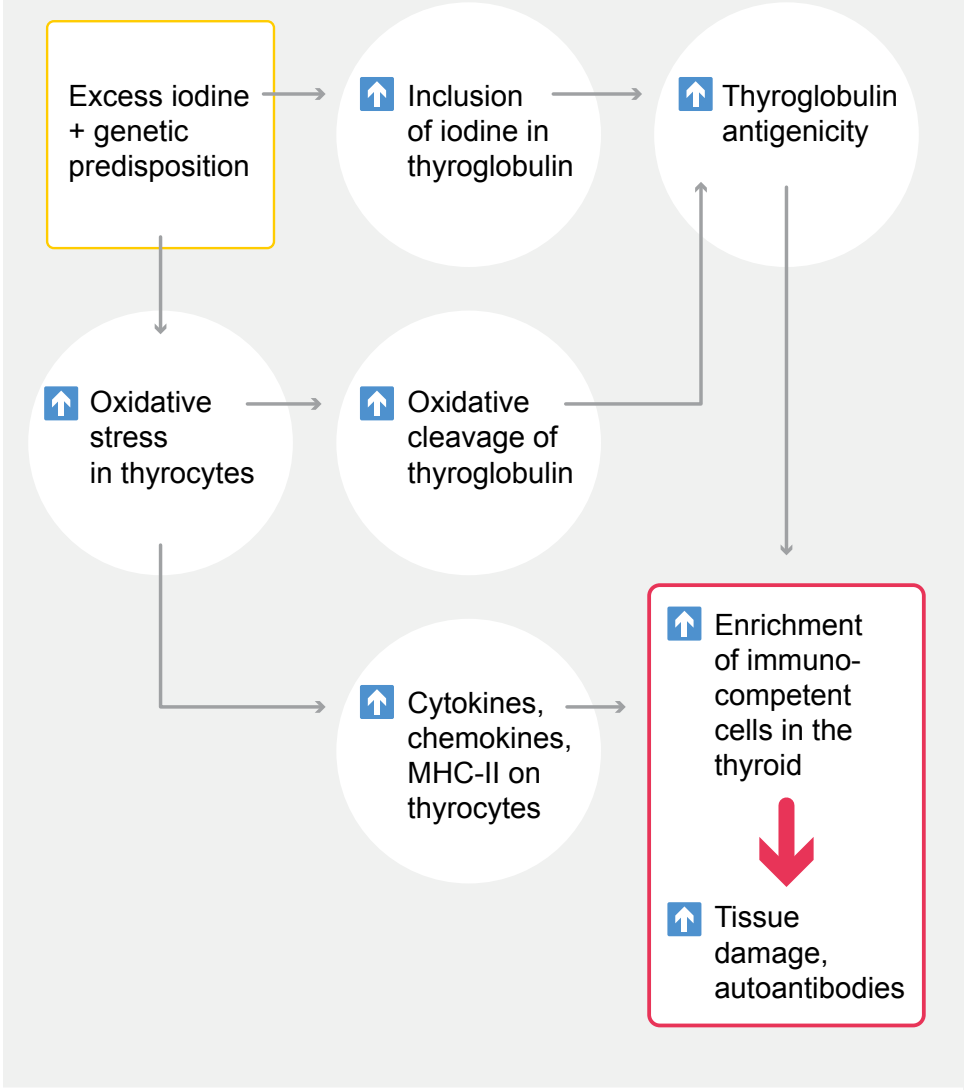
Selenium can positively influence the negative effects of excess iodine on the thyroid

Conversely, however, the prevalence of chronic thyroiditis has significantly increased. Not only an iodine deficit, but also an iodine surplus can lead to pathological changes in the thyroid. Depending on the dosage, iodine stimulates autoimmune damage to the thyroid by diverse mechanisms *(Fig. 6)*.[10]

Excess iodine increases oxidative stress on the thyrocytes. Reactive oxygen species (ROS) are ordinarily required for the oxidation of iodine or its organification. An iodine surplus deregulates this process and leads to cellular damage by ROS. The additional consequences are pro-inflammatory changes which lead to increased production of cytokines and chemokines. Changes in the thyrocytes occur as well. The expression of the so-called MHC II complex is increased on the cell surface, and intracellularly, the adhesion molecule ICAM-1 is increasingly produced.

The consequence of this process is an increase of autoantigenicity of thyroglobulin, which attracts immunocompetent cells. This leads to an infiltration by immune cells and the production of autoantibodies in the thyroid. The consequence of this development is an autoimmune thyroiditis.[10]

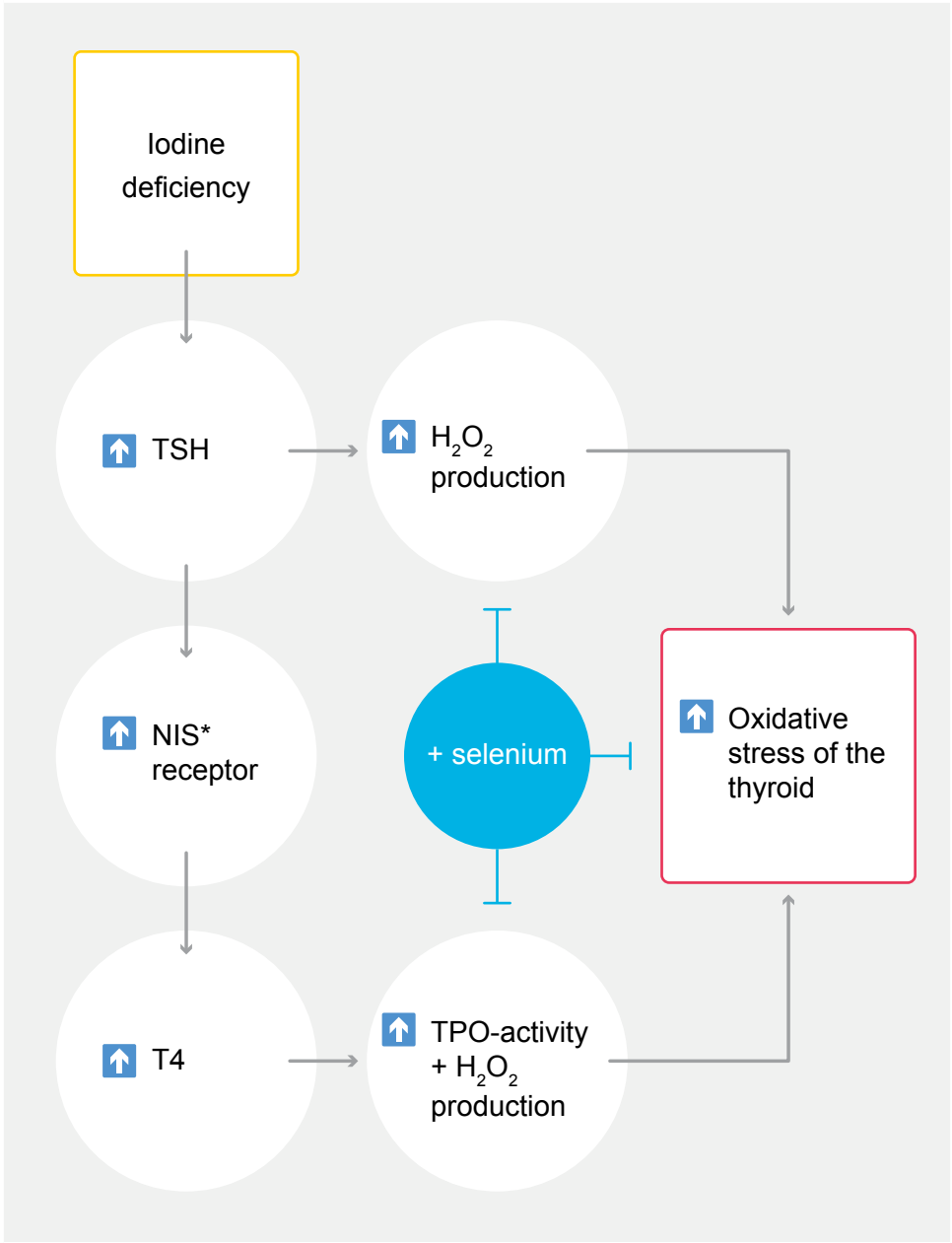
Selenium can positively influence the negative impact of excess iodine on the thyroid



Prete A, Paragliola RM, Corsello SM. Int J Endocrinol. 2015; 2015: 312305. doi: 10.1155/2015/312305. Iodine Supplementation: Usage "with a Grain of Salt"

Fig. 6

Only an adaptation of the selenium supply to increased oxidative stress due to an iodine deficiency can protect the thyroid



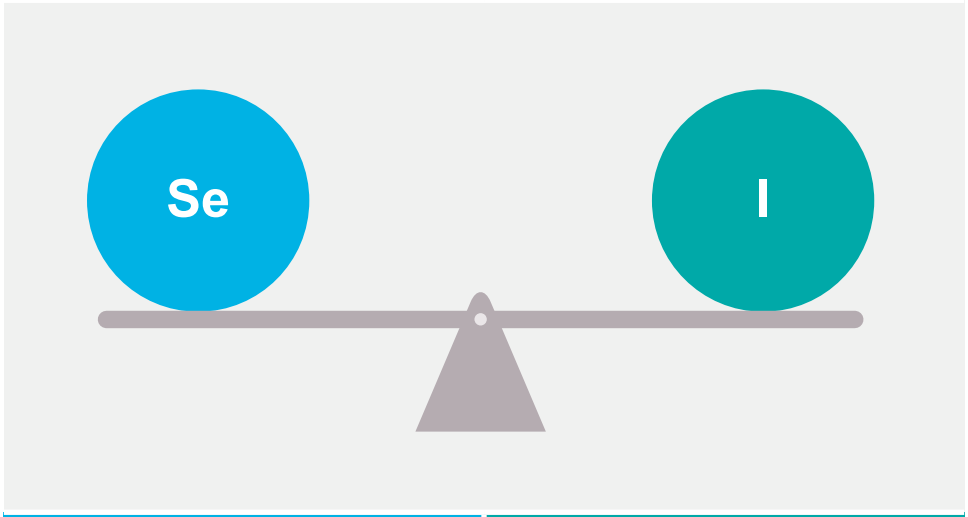
* NIS = sodium iodide symporter

Arthur JR, Beckett GJ, Mitchell JH. Nutr Res Rev. 1999 Jun; 12(1): 55-73. The interactions between selenium and iodine deficiencies in man and animals.

Spitzweg C, Morris JC. Hormones (Athens). 2002 Jan-Mar; 1(1): 22-34. Sodium iodide symporter (NIS) and thyroid.

Fig. 7

The thyroid requires balance between selenium and iodine



Selenium	Iodine
• Essential for thyroid metabolism	• Essential component for thyroid hormones
• Recommended daily intake: 70 µg per day	• Recommended daily intake: 150 µg per day
• Protects the thyroid from oxidative stress	• Iodine surplus can promote oxidative stress

Fig. 8

Only an adaptation of the selenium supply can protect the thyroid from the increased oxidative stress due to an iodine deficit

Independent of whether the increased oxidative stress in the thyroid is triggered by an iodine deficiency or iodine surplus, the breakdown of the ROS selenoproteins is necessary, because the selenium-dependent glutathione-peroxidases reduce ROS and protect the thyroid tissue from oxidative damage *(Fig. 6, 7)*.[3, 10] It can therefore be assumed that a sufficient selenium supply prevents an increased number of autoimmune thyroiditis incidences.[11]

If both a selenium deficiency as well as an inadequate iodine supply is the case, the negative effects rapidly increase. Despite an optimal iodine supply, the thyroid is oxidatively attacked at low selenium status. The balance between selenium and iodine is therefore crucial for a healthy thyroid *(Fig. 8)*.

Pregnancy, thyroid and selenium

At a glance
Increased risk for thyroid disorder during pregnancy
Thyroid disorders have far-reaching consequences for mother and child
Negative impact of hypothyroidism on the brain development of the baby
Risk screening identifies only 20 percent of those affected
Selenium reduces the risk of postpartum thyroiditis of TPO antibody-positive pregnant women
Selenium reduces the postpartum TPO antibody titer
Selenium stops the postpartum deterioration of thyroiditis
Selenium deficiency increases the risk of pre-eclampsia
Selenium supplementation reduces the risk of pre-eclampsia
Selenium deficiency increases the risk of premature birth
Selenium supplementation protects against postpartum depression
Lower selenium status during pregnancy negatively influences the development of the baby

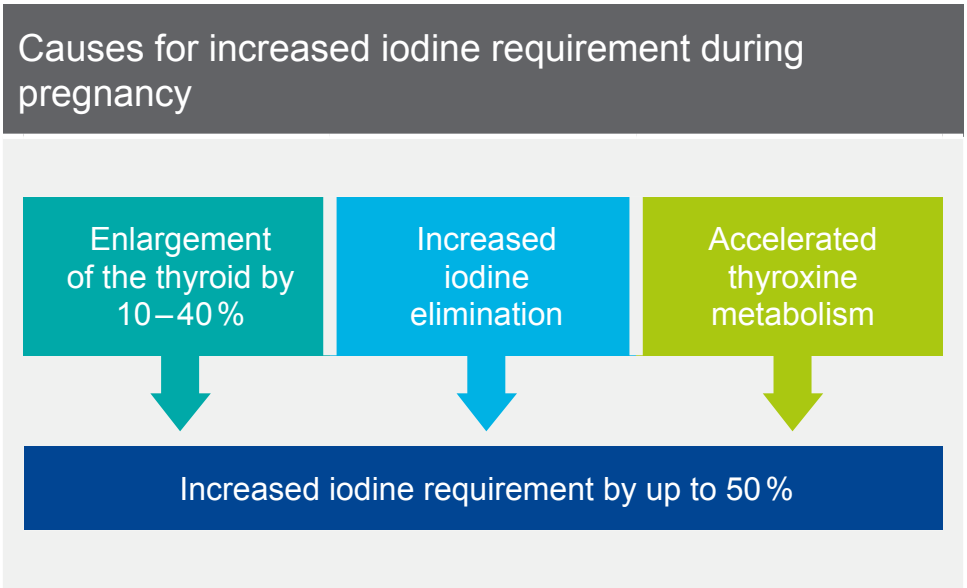


Fig. 9

Pregnancy has a large impact on the thyroid

During pregnancy, the entire women's body is exposed to great additional stresses – the thyroid as well. The small organ works at full speed in order to adjust to the changed circumstances. This can lead to thyroid dysfunction which, untreated, has far-reaching consequences for mother and child.

The thyroid grows in the course of pregnancy: in countries with a good iodine supply, it increases its size by about ten percent – even 20 to 40 percent in regions with iodine deficiency.[12] The most important change in the metabolism of the thyroid is the increased need for thyroid hormones.[13] The TSH level is reduced during pregnancy due to the stimulating effect of the human chorionic gonadotropin hormone at the TSH receptor.[14] Increased production of thyroid hormones as well as increased iodine elimination raise the iodine requirement by up to 50 percent *(Fig. 9)*.[14]

Increased risk of thyroid disorders during pregnancy

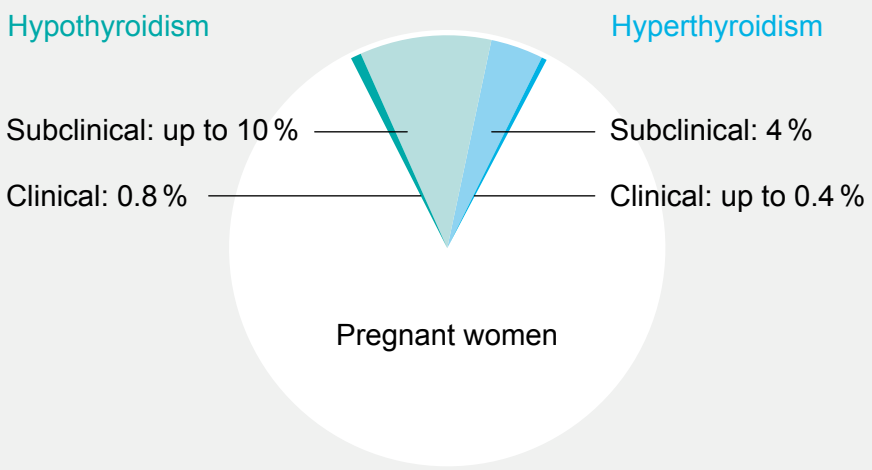
The physiological changes in women with an iodine deficiency can show normal thyroid function in the first trimester of pregnancy, but lead to hypothyroidism in the further course of pregnancy. [12] Clinical hypothyroidism occurs in about 0.4 percent of pregnant women. The frequency of subclinical hypothyroidism is significantly higher at three to ten percent. Hypothyroidism remains permanently for many of the affected women.[12] Autoimmune thyroiditis is one of the most frequent causes.[14]

A little less frequently, pregnant women develop clinical hyperthyroidism (0.1 to 0.4 percent).[14] A subclinical hyperthyroidism affects about four percent of pregnant women. Graves' disease and gestation hyperthyroidism are among the frequent causes.[14] Thus, up to 15 percent of pregnant women are affected by a thyroid disorder *(Fig. 10)*.

Risk factor TPO antibody

About 10 percent of pregnant women are TPO antibody-positive and euthyroid. [15] Half of the pregnant women with increased TPO antibodies developed postpartum thyroiditis *(Fig. 11)*. In turn, 40 percent of the women with a postpartum thyroiditis develop a permanent hypothyroidism.[15] The prevalence of postpartum thyroiditis in TPO antibody-negative pregnant women is significantly lower with 7.2 percent.[15]

Up to 15 percent of pregnant women are affected by thyroid disorders

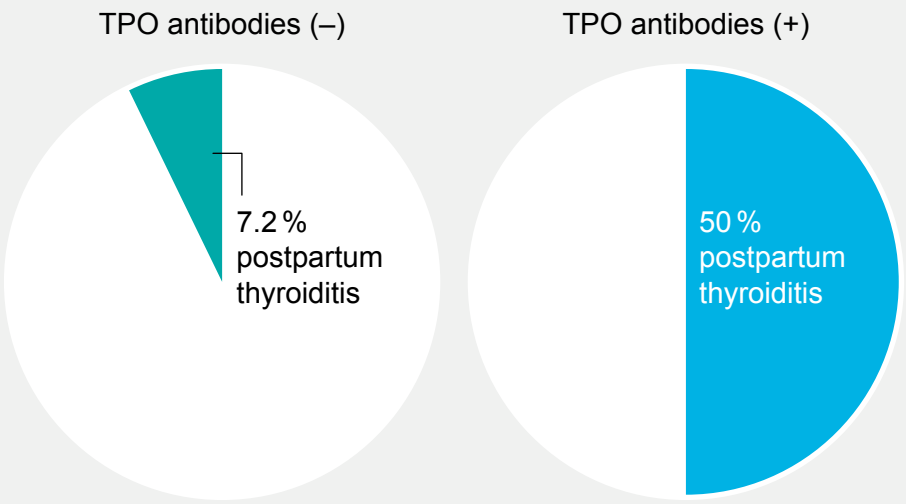


Stagnaro-Green A, Abalovich M, Alexander E, et al. Thyroid. 2011 Oct; 21(10): 1081-1125. doi: 10.1089/thy.2011.0087. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum.

Führer D, Mann K, Feldkamp J, Krude H, Spitzweg C, Kratzsch J, Schott M. Dtsch Med Wochenschr. 2014 Oct; 139(42): 2148-2152. doi: 10.1055/s-0034-1387300. Thyroid dysfunction in pregnancy.

Fig. 10

Risk factor TPO antibodies in pregnancy



Negro R, Greco G, Mangieri T, et al. J Clin Endocrinol Metab. 2007 Apr; 92(4): 1263-1268. The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase autoantibodies.

Fig. 11

Thyroid disorders have far-reaching consequences for mother and child

If thyroid disorders during pregnancy are not recognized and treated in a timely manner, they can have far-reaching consequences for mother and child.[16] This applies both to thyroid hypofunction as well as hyperfunction *(Table 1)*. Both increase the risk of spontaneous miscarriage as well as early and stillbirth. Also the risk of pre-eclampsia is increased with a thyroid dysfunction.

Hypothyroidism impairs the cognitive development of a child. This can lead to congenital cretinism with deafness and neuropsychological impairments. Screening trials show that the birth and healthy development of about 3,500 children in Germany are annually at risk for clinical hypothyroidism.[14]

Congenital heart malformations in the baby can be the consequence of hyperthyroidism in the mother. The risk is not only increased for pregnant women with a thyroid disorder. Also babies of euthyroid pregnant women with subclinical thyroiditis already have a higher risk of heart malformations.[12, 14]

Hypothyroidism during pregnancy impairs the cognitive development of the child

Possible consequences of thyroid disorder in mother and child

Hyperthyroidism	
Mother's increased risk for	**Child's increased risk for**
• Spontaneous miscarriage as well as premature birth and stillbirth	• Low birth weight
• Cardiac insufficiency	• Congenital malformation of the heart
• Pre-eclampsia	
• Thyrotoxic crisis (very rare)	

Hypothyroidism	
Mother's increased risk for	**Child's increased risk for**
• Spontaneous miscarriage as well as premature birth and stillbirth	• Perinatal disorder and mortality
• Increased blood pressure in pregnancy	• Impairment of cognitive development
• Pre-eclampsia	• Congenital cretinism with deafness and neuropsychological impairments
• Placenta detachment	
• Anemia	• Low birth weight

Reid SM, Middleton P, Cossich MC, et al. Cochrane Database Syst Rev. 2013 May 31;5:CD007752. doi: 10.1002/14651858.CD007752.pub3. Interventions for clinical and subclinical hypothyroidism pre-pregnancy and during pregnancy.

Führer D, Mann K, Feldkamp J, Krude H, Spitzweg C, Kratzsch J, Schott M. Dtsch Med Wochenschr. 2014 Oct;139(42):2148-52. doi: 10.1055/s-0034-1387300. Thyroid dysfunction in pregnancy.

Table 1

Negative impact of hypothyroidism on the brain development of the baby

Already in 1999, Haddow et al. could show that an untreated hypothyroidism in the mother significantly increases the risk of a reduced IQ in the child (7 points lower; $p = 0.005$).[17] Nineteen percent of the children showed an IQ of ≤ 85, whereas it was only 5 percent in the control group.

But not only a clinical hypothyroidism has an impact on the brain development of the baby. Already a subclinical hypothyroidism has this effect, as shown in a trial from 2010 *(Fig. 12)*.[18] Both the IQ as well as the motoric levels were significantly lower (IQ 8.9 points lower [$p = 0.008$] or 10 points lower [$p < 0.001$]).

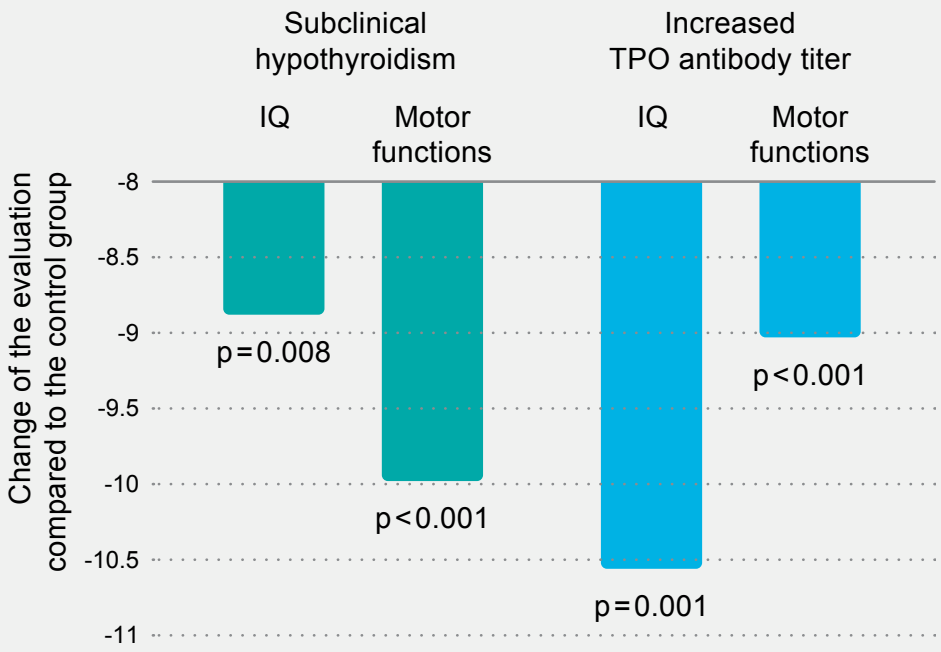
The values of the babies between 25 and 30 months from euthyroid mothers with increased TPO antibodies were also determined in this trial. The mean IQ was reduced by 10.6 points ($p = 0.001$). The levels for the motor functions were 9 points lower ($p < 0.001$).

Increased TPO antibody titer increases the risk for hyperactivity

An additional trial could demonstrate the relationship between the maternal thyroid function and the development of the child.[19] In the so-called Generation R trial, 3,139 children between 2.5 and 3 years as well as their mothers were investigated. Increased TPO antibody titer of the mother led to an increased risk of attention deficiency disorder (ADD) or hyperactivity (Odds Ratio = 1.77; 95 % CI 1.15 – 2.72; $p = 0.01$).

The authors point out that the impact of the results cannot be evaluated since there is no specific treatment for TPO antibody positive pregnant women with normal thyroid function to date.

Changed thyroid parameters of the mother negatively influence the development of the baby



Li Y, Shan Z, Teng W, et al. Clin Endocrinol (Oxf). 2010 Jun; 72(6): 825-829. doi: 10.1111/j.1365-2265.2009.03743.x. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25-30 months.

Fig. 12

Risk screening identifies only 20 percent of those affected

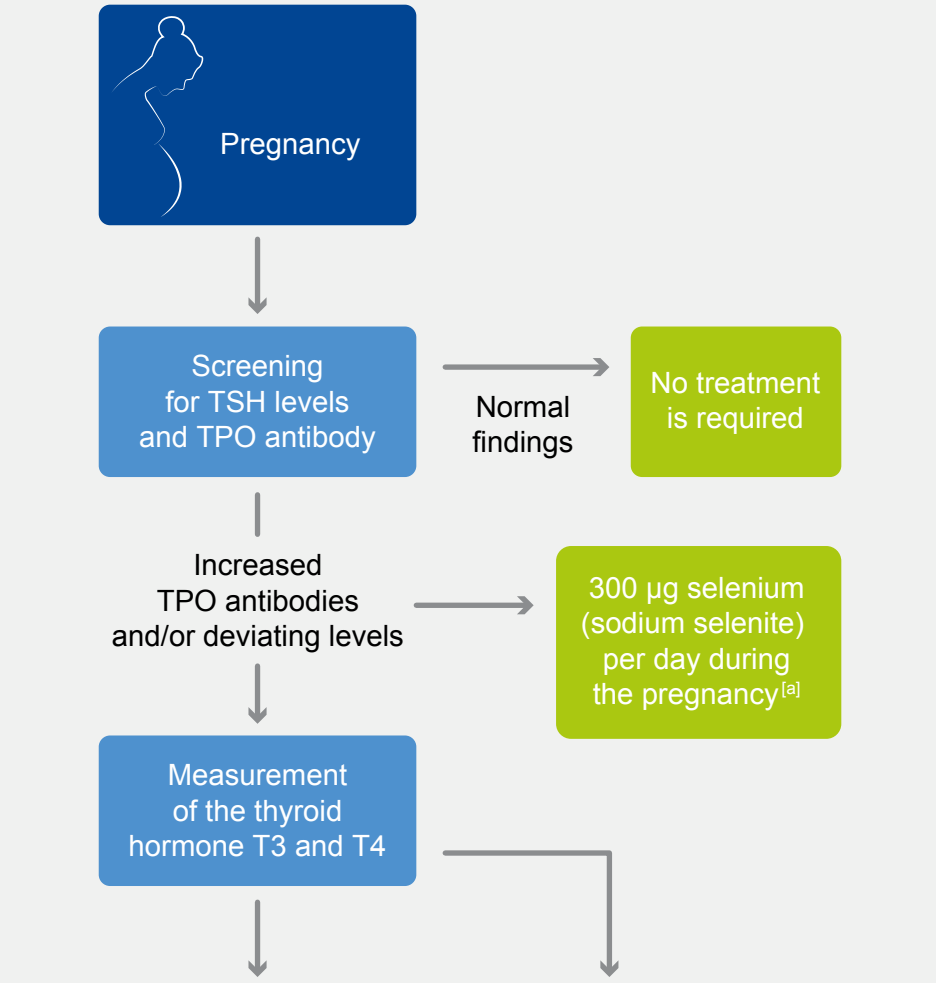
A trial conducted by Chang et al. (2011) concluded that general screening is appropriate, since only 20 percent of thyroid problems are diagnosed in a risk-oriented screening.[20] An additional trial could confirm this result.[21] The German maternity guidelines so far do not include general thyroid screening.[22] The thyroid is therefore not routinely investigated for malfunctions, but only if there is a specific suspicion.[15] However, the current guidelines of the European Thyroid Association (ETA) from 2014 recommend the universal screening of pregnant women.[23]

The screening should at least encompass the TSH level, ideally also the TPO antibody titer.[14] Screening at the gynecological determination of pregnancy is recommended, since the brain development of the baby already begins at a very early point in time and is dependent on the supply of maternal thyroid hormones.

In the event of deviating TSH levels, a measurement of the T4 and T3 levels, a determination of the TR and TPO antibodies as well as an ultrasound examination are appropriate.[14] If the findings are abnormal, the physician should regularly check thyroid levels *(Fig. 13)*.[14]

The European Thyroid Association recommends universal thyroid screening of pregnant women

Model for thyroid screening in pregnant women



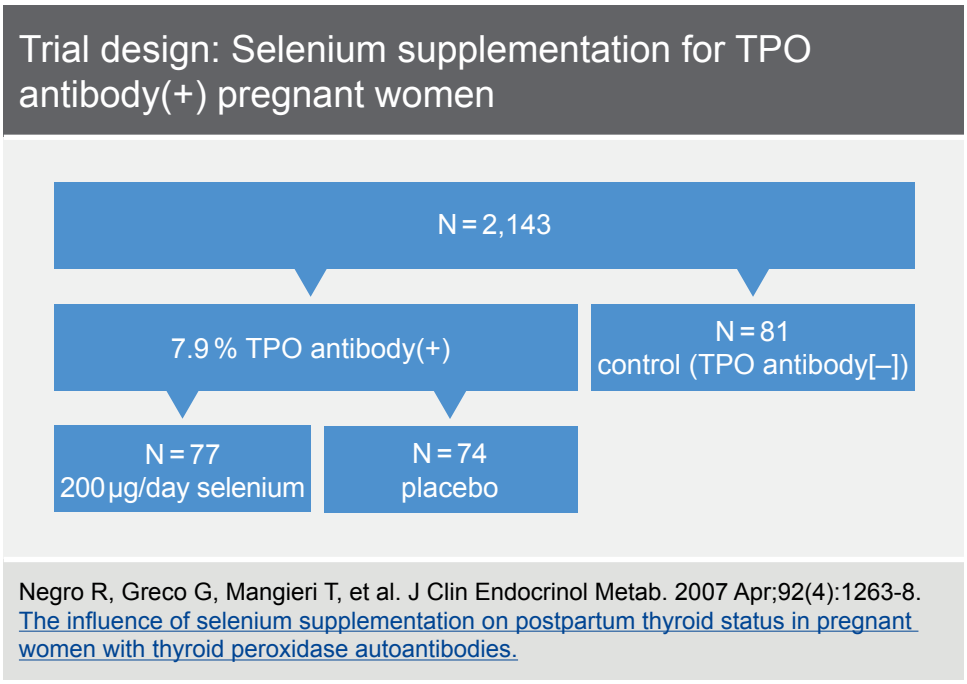
[a] Tolerable upper intake levels for vitamins and minerals. Scientific Committee on Food Scientific Panel on Dietetic Products, Nutrition and Allergies, February 2006.

[b] Procedure for reduced TSH values.

[c] Procedure for increased TSH values.

Modified according to Führer D et al. Dtsch Med Wochenschr. 2014 Oct; 139(42): 2148-52. Thyroid dysfunction in pregnancy.

Fig. 13



Negro R, Greco G, Mangieri T, et al. J Clin Endocrinol Metab. 2007 Apr;92(4):1263-8. The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase autoantibodies.

Fig. 14

Selenium therapy for pregnant women with thyroiditis

In a prospective, randomized, placebo-controlled trial, 2,143 pregnant women with normal thyroid function were investigated. 7.9 percent of the pregnant women were TPO antibody-positive *(Fig. 14)*.[15] During the pregnancy and the postpartum period, 77 TPO antibody-positive pregnant women were supplemented with 200 µg selenium per day, while 74 TPO antibody-positive pregnant women received a placebo. These two groups were compared to a control group of 81 TPO antibody-negative pregnant women.

Selenium reduces the risk of postpartum thyroiditis in TPO antibody-positive pregnant women

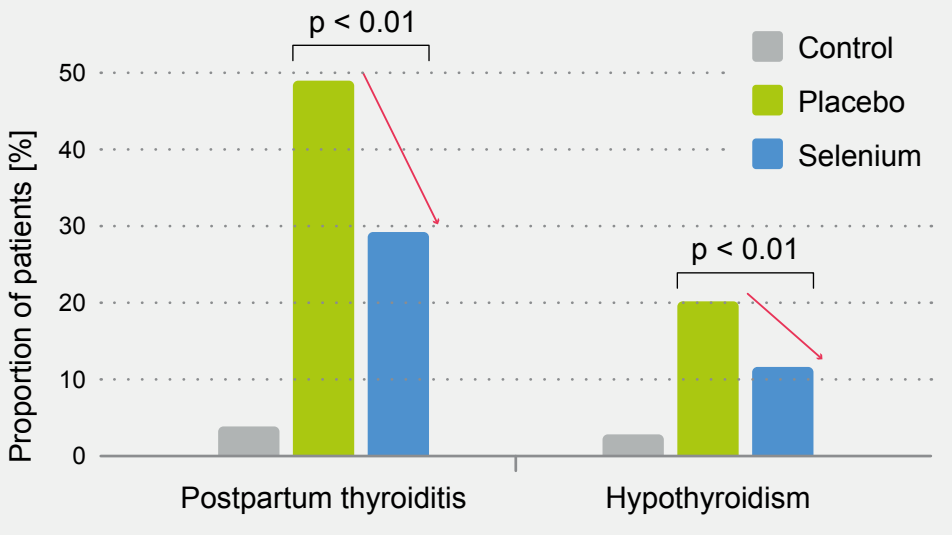
The study by Negro et al. confirms that 50 percent of TPO antibody-positive pregnant women develop thyroiditis (48.6 percent).[15] In the group supplemented with selenium, the proportion was reduced by 20 percent to 28.6 percent ($p < 0.01$) *(Fig. 15)*. Also, selenium therapy reduced the development of permanent hypothyroidism significantly from 20.3 percent to 11.7 percent ($p < 0.01$).

Selenium reduces the postpartal TPO antibody titer

During pregnancy, there are significant changes in the TPO antibody titer. Selenium therapy significantly reduces the concentrations of TPO antibodies compared to placebo (62.4 % vs. 43.9 %; $p < 0.01$).[15] After the pregnancy, the TPO antibody status at TPO antibody-positive women significantly increased again. The supplementation with selenium significantly attenuated this increase (383.4 ± 1.48 kIU/l vs. 745.5 ± 257 kIU/l; $p < 0.01$).

During the entire postpartum time period, the TPO antibody titer in the selenium supplemented group was significantly lower ($p < 0.01$) *(Fig. 16)*.

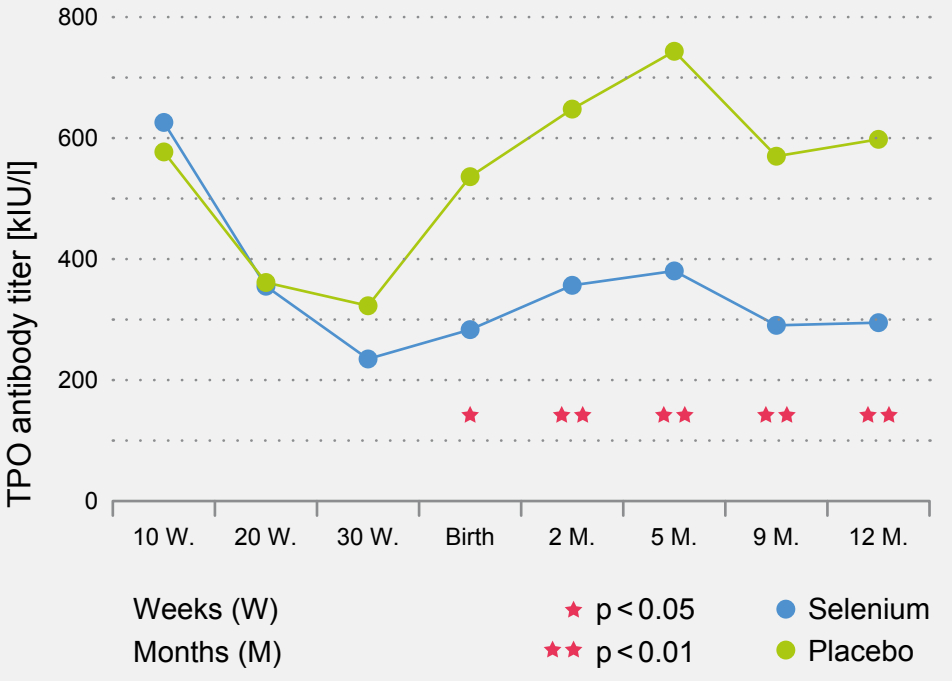
Selenium reduces the risk of postpartum thyroiditis in TPO antibody-positive pregnant women



Modified according to Negro R, Greco G, Mangieri T, et al. J Clin Endocrinol Metab 2007; 92: 1263-1268. The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase autoantibodies.

Fig. 15

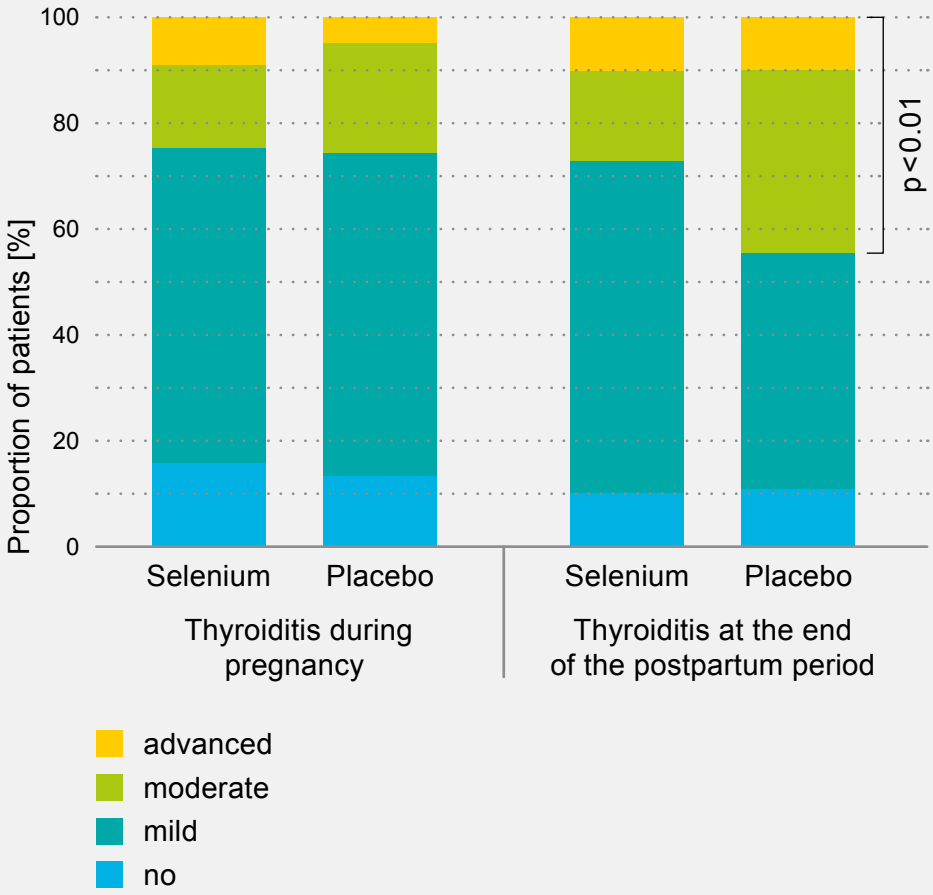
Selenium reduces the postpartal TPO antibody titer



Modified according to Negro R, Greco G, Mangieri T, et al. J Clin Endocrinol Metab 2007; 92: 1263-1268. The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase autoantibodies.

Fig. 16

Selenium inhibits the postpartum deterioration the thyroiditis

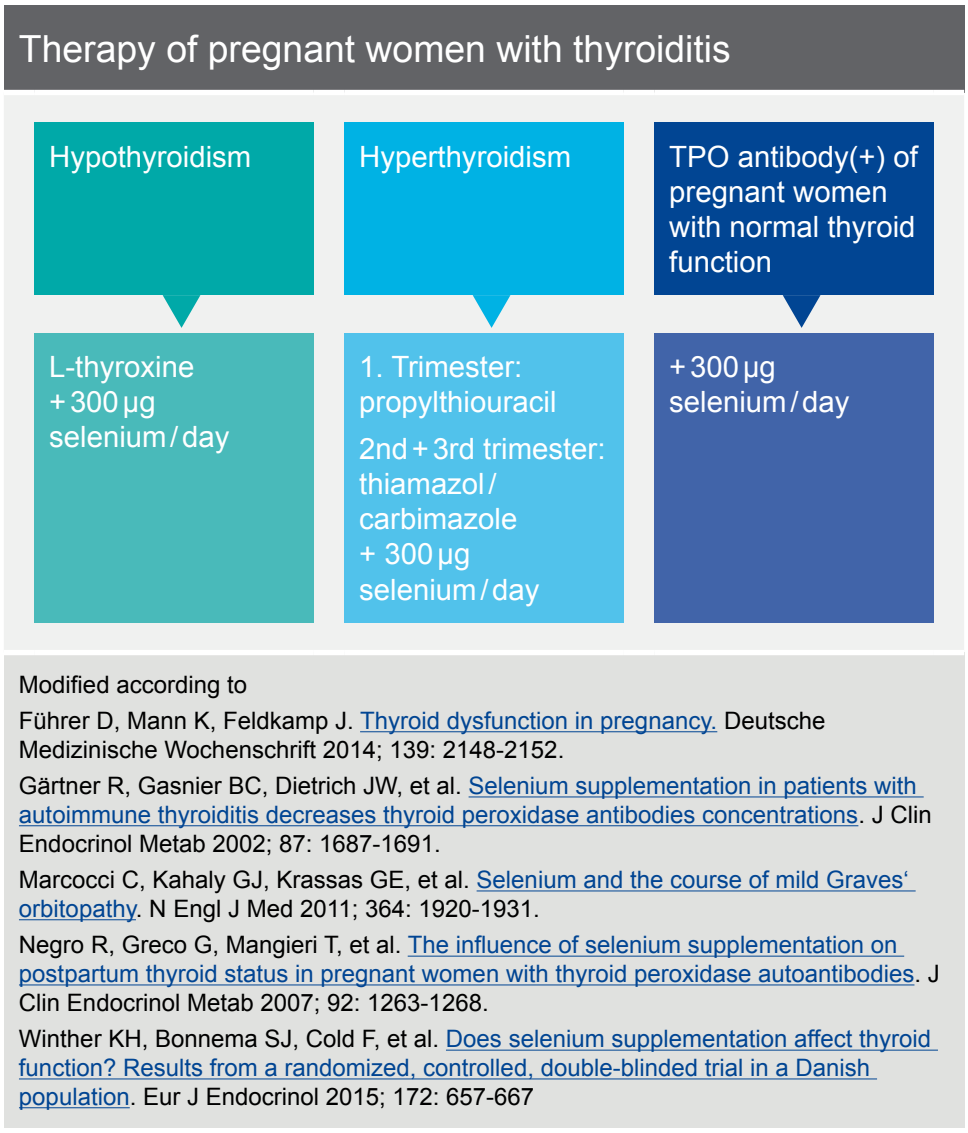


Negro R, Greco G, Mangieri T, et al. J Clin Endocrinol Metab. 2007 Apr; 92(4): 1263-1268. The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase autoantibodies.

Fig. 17

Selenium inhibits the postpartum deterioration of thyroiditis

In addition, Negro et al. investigated the echogenicity of the thyroid during pregnancy, at birth and after 12 months.[15] At the end of the postpartum period, most participants of the selenium-supplemented group had no or only mild thyroiditis (72.7 % vs. 55.4 %). However in the placebo group, a majority showed a moderate or advanced thyroiditis (44.6 % vs. 27.3 %; $p < 0.01$) *(Fig. 17)*. Moreover, the echogenicity of the thyroid significantly only deteriorated in the placebo group ($p < 0.05$).



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Gärtner R, Gasnier BC, Dietrich JW, et al. Selenium supplementation in patients with autoimmune thyroiditis decreases thyroid peroxidase antibodies concentrations. J Clin Endocrinol Metab 2002; 87: 1687-1691.

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Winther KH, Bonnema SJ, Cold F, et al. Does selenium supplementation affect thyroid function? Results from a randomized, controlled, double-blinded trial in a Danish population. Eur J Endocrinol 2015; 172: 657-667

Fig. 18

Therapy of pregnant women with thyroiditis

The treatment of a thyroid dysfunction in pregnancy depends on the form and degree of severity *(Fig. 18)*. A selenium therapy with 300 µg selenium in form of sodium selenite is possible without problems during pregnancy and lactation. According to the EU, a daily intake of 300 µg selenium is possible for pregnant women without any adverse reactions.[33]
A combination of selenium with L-thyroxine or thyrostatic substances is unproblematic.

Selenium deficiency in pregnancy

A selenium supplementation during pregnancy helps in the treatment and prevention of thyroiditis. Additionally, a selenium deficiency as such has far-reaching consequences for mother and child. In Germany the selenium supply is suboptimal. Latest trials have determined a mean serum selenium concentration of 73.2 µg/l for healthy women.

Selenium deficiency increases the risk of pre-eclampsia

Pre-eclampsia is one of the pregnancy disorders accompanied by high blood pressure. It occurs in about two to seven percent of all pregnancies and, in the western world, is the most frequent reason for mortality and morbidity of mother and child. Together with other pregnancy disorders such as high blood pressure, the perinatal mortality increases five-fold.[24, 25]

A global trial investigated the data of almost 6.5 million births.[26] The global incidence of pre-eclampsia was 3.5 percent and thus concerned more than 220,000 births. With declining selenium status the frequency of pre-eclampsia increased significantly ($p < 0.0001$). The comparison of the pre-eclampsia incidence at a cut-off level of 95 µg/l showed that for a serum selenium concentration below this level, pre-eclampsia frequency significantly increases ($p < 0.0007$) *(Fig. 19)*.

Why 95 µg/l selenium in the serum? – This level conforms with the selenium concentration in the serum at which the selenoprotein glutathione peroxidase 1 achieves maximum activity and an adequate selenium supply can be assumed. At the same time, the result means that no selenium deficiency must be present in order to increase the risk of pre-eclampsia, since in Germany a selenium deficiency begins at below 80 µg/l selenium in the serum *(Fig. 20)*.

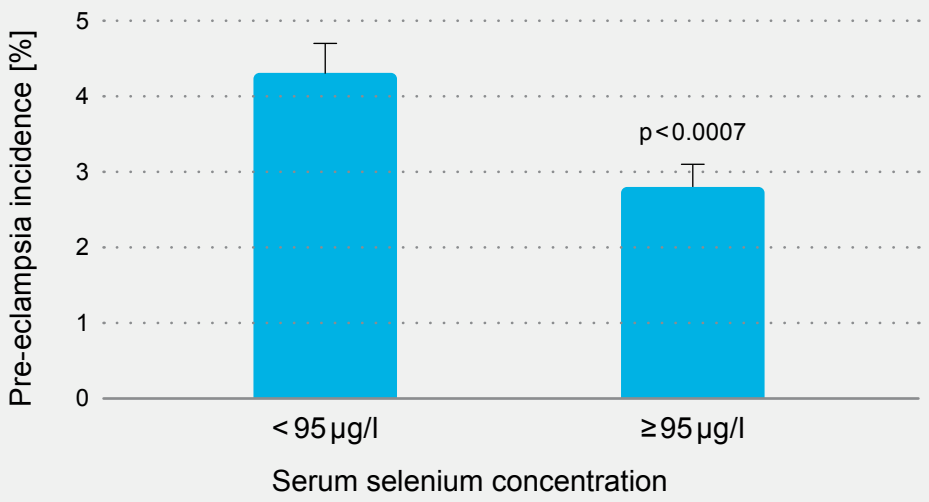
Selenium supplementation reduces the risk of pre-eclampsia

In the so-called SPRINT trial (double-blind, placebo-controlled pilot study), 230 pregnant women were supplemented either with 60 µg selenium per day or a placebo.[27] The trial was carried out in Great Britain. At the beginning of the trial, the participants showed a selenium concentration of 104.2 µg/l selenium in whole blood. The pregnant women were thereby rated as having borderline selenium deficiency (< 100 µg/l). The selenium supplementation reduced the risk of pre-eclampsia or a pregnancy induced high blood pressure by 70 percent (OR 0.3; 95 % CI 0.09 – 1.00; $p = 0.049$).

Selenium deficiency increases the risk of premature birth

In a prospective Danish trial, the pregnancy of almost 1,200 women was investigated.[28] Sixty pregnant women (5.3 percent) had a premature birth. The serum selenium concentration in the twelfth pregnancy week of women with a premature birth was significantly lower (75.8 ± 11.1 µg/l vs. 80.5 ± 10.3 µg/l; $p = 0.001$). The women with the lowest selenium levels had twice as high a risk of premature birth after a correction due to pre-eclampsia (OR 2.18; 95 % CI 1.25 – 3.77).

Increased pre-eclampsia incidence at low selenium status



Vanderlelie J, Perkins AV. Pregnancy Hypertens. 2011 Jul-Oct;1(3-4):213-24. doi: 10.1016/j.preghy.2011.07.001. Selenium and preeclampsia: A global perspective.

Abb. 19

Increased risk for pre-eclampsia already significant in the German reference range

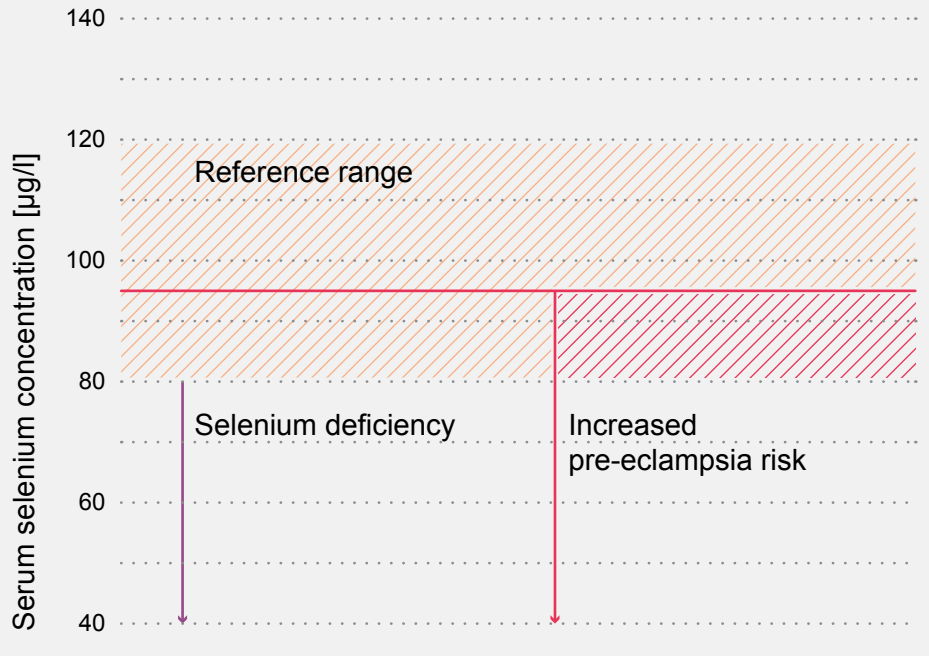


Fig. 20

Selenium supplementation reduces the risk of postpartum depressions

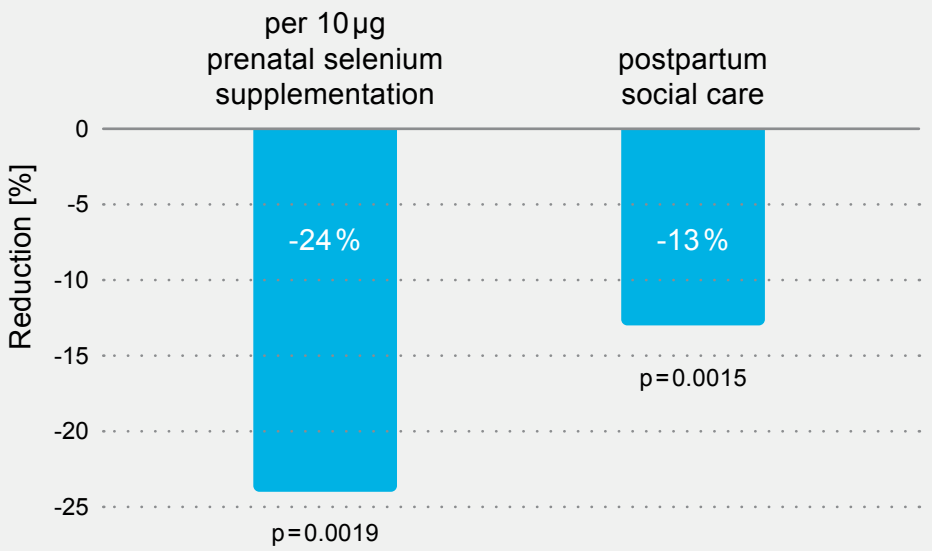
Between ten and fifteen percent of women suffer from postpartum depression.[29] Aside from a genetic predisposition, the risk factors include environmental, social, psychological and biological factors. The biological factors include inadequate diet. In the so-called APrON trial, 475 participants were investigated for the relationship between postpartum depression based on the "Edinburgh Postpartal Depression Scale" (EPDS) and their micronutrient intake.[29]

Twelve percent of the participants showed an EPDS of ≥ 10 and thus a postpartum depression. At low EPDS, the selenium intake was significantly higher ($p = 0.0015$). At the determination of predictive factors for postpartum depression only the perinatal intake of selenium above the RDA recommendation (55 µg) could reduce the risk. For each 10 µg selenium, the risk declined by 24 % (OR 0.76; 95 % CI 0.74 – 0.78; $p = 0.019$) *(Fig. 21)*.[29] In comparison: the positive effect of social support reduced the risk by 13 % (OR 0.85; 95 % CI 0.74 – 0.97; $p = 0.015$).

Lower selenium status during pregnancy negatively influences the development of the baby

The selenium status and the development of the baby was investigated in a prospective cohort study of 750 mothers.[30] The children aged 1.5 years were evaluated on their mental and psychomotoric development as well as their language understanding and their mode of expression. In this trial, the selenium concentration in the erythrocytes was measured as degree for the long-term selenium status. An increase of the selenium by 0.5 g for each gram of hemoglobin improved the language understanding by 3.7 points ($p = 0.028$). For girls, the psychomotoric development improved by 12 points ($p = 0.002$) *(Fig. 22)*.

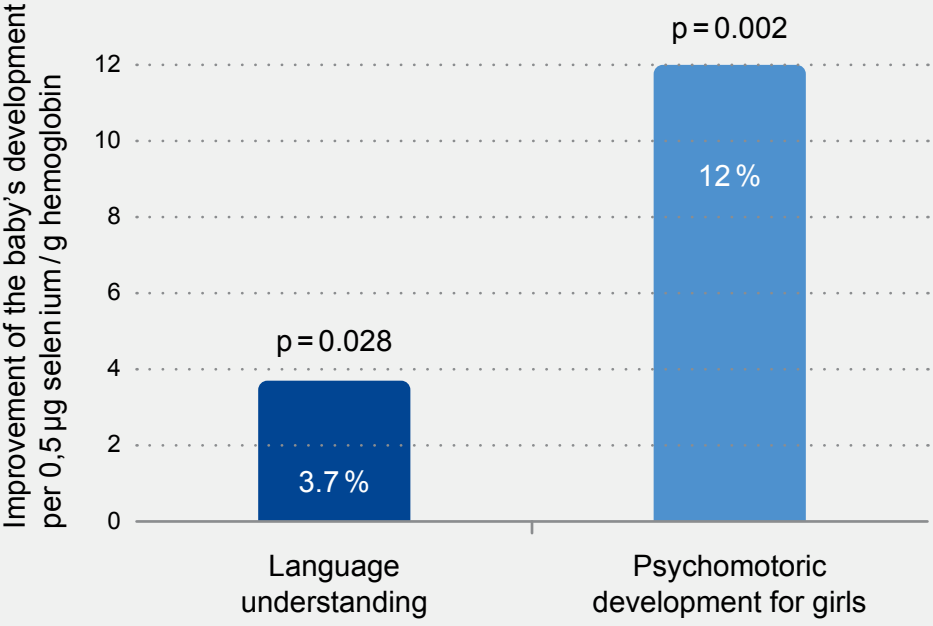
Selenium supplementation reduces postpartum depression



Leung BM, Kaplan BJ, Field CJ, et al. BMC Pregnancy Childbirth. 2013 Jan 16; 13: 2. doi: 10.1186/1471-2393-13-2. Prenatal micronutrient supplementation and postpartum depressive symptoms in a pregnancy cohort.

Fig. 21

Selenium supplementation during pregnancy can positively influence the development of the baby



Skröder HM, Hamadani JD, Tofail F, et al. Clin Nutr. 2015 Oct; 34(5): 923-930. doi: 10.1016/j.clnu.2014.09.020. Selenium status in pregnancy influences children's cognitive function at 1.5 years of age.

Fig. 22

Overview of trials: pregnancy, thyroid and selenium

Leung BM, Kaplan BJ, Field CJ, Tough S, Eliasziw M, Gomez MF, McCargar LJ, Gagnon L; APrON Study Team

Prenatal micronutrient supplementation and postpartum depressive symptoms in a pregnancy cohort

BMC Pregnancy Childbirth 13:2 (2013)

With 475 women, the APrON trial recorded the micronutrient intake (every trimester + 12 weeks postpartal) and postpartum depressions (based on the "Edinburgh Postnatal Depression Scale" [EPDS]). Twelve percent of the women showed a postpartum depression of (EPDS ≥ 10). Women with higher selenium intake had significantly lower EDPS levels ($p = 0.0015$). Prenatal intake of selenium supplements significantly reduced the risk of postpartum depression per 10 µg selenium (OR 0.76, 95 % CI 0.75 – 0.78; $p = 0.0019$).

Negro R, Greco G, Mangieri T et al.

The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase antibodies

Clin Endocrinol Metab 2007; 92(4):1263–1268

In the prospective, randomized, placebo-controlled trial, 2,143 pregnant women with normal thyroid function were tested for TPO antibodies. 7.9 percent were TPO antibody-positive. Seventy-seven of the pregnant women screened positive were supplemented with 200 µg selenium daily during pregnancy and postpartum, 74 of the TPO antibody-positive pregnant women received a placebo. In the selenium group, both the postpartum thyroid dysfunction (28.6 % versus 48.6 %; $p < 0.01$) As well as the prolonged hypothyroidism (11.7 % versus 20.3 %; $p < 0.01$) were significantly reduced.

www.ncbi.nlm.nih.gov/pubmed/17284630

Rayman MP, Searle E, Kelly L et al.

Effect of selenium on markers of risk of pre-eclampsia in UK pregnant women: a randomised, controlled pilot trial

Brit J Nutr 2014; 112:99–111

230 primiparous women received either 60 µg selenium per day or a placebo from the period between the twelfth and the 14th pregnancy week. After 35 weeks, the selenium level in the selenium group had significantly increased and the risk marker of pre-eclampsia was significantly lower than in the control group. The authors came to the conclusion that even a minor increase of selenium intake could reduce the risk of pre-eclampsia.

www.ncbi.nlm.nih.gov/pubmed/24708917

Rayman MP, Wijnen H, Vader H, Kooistra L, Pop V

Maternal selenium status during early gestation and risk for preterm birth

CMAJ 183 (2011) 549-555

1,197 Danish women were prospectively accompanied during their pregnancy. The selenium status was measured in the 12th pregnancy week. Sixty women (5.3 percent) had a premature birth. The serum selenium concentration of women with premature birth was significantly lower ($p = 0.001$). After classification of the women in quartiles according to their serum selenium concentration, the women in the quartile with the lowest selenium levels had a risk twice as high as the women in the three other quartiles (OR 2.18; 95 % CI 1.25 – 3.77). The authors concluded from this data that a lower selenium status at the end of the first trimester increases the risk of a premature birth.

Rayman MP, Bath SC, Westaway J et al.

Selenium status in UK pregnant women and its relationship with hypertensive conditions of pregnancy

Brit J Nutr 2015; 113:249–258

From the period between the twelfth and the 14th pregnancy week to the delivery, 230 primiparous women received either 60 µg selenium per day or a placebo. The selenium supplementation reduced the risk of pre-eclampsia and pregnancy-related hypertension.

www.ncbi.nlm.nih.gov/pubmed/25571960

Reid SM, Middleton P, Cossich MC et al.

Interventions for clinical and subclinical hypothyroidism pre-pregnancy and during pregnancy

Cochrane Database Syst Rev. 2013 May 31;5:CD007752. doi: 10.1002/14651858.CD007752.pub3

This is a meta-analysis of four randomized controlled trials with a total of 362 women. The treatment of hypothyroiditis and subclinical hypothyroiditis in pregnancy was investigated. None of the trials reported a delay in neurological development. With levothyroxine treatment an insignificant trend for less miscarriages was seen. Selenium showed a positive effect on the postpartum thyroid function and reduced the incidence of moderate to advanced postpartum thyroiditis.

www.ncbi.nlm.nih.gov/pubmed/23728666

Skröder HM, Hamadani JD, Tofail F, Persson LÅ, Vahter ME, Kippler MJ

Selenium status in pregnancy influences children's cognitive function at 1.5 years of age

Clin Nutr 34 (2015) 923-390

In this prospective cohort study, the selenium status of 750 women and the development of their children was investigated. The mental and psychomotoric development as well as language understanding and mode of expression of the children was evaluated at 1.5 years of age. The selenium concentration was measured in the erythrocytes. Language understanding of children improved by 3.7 points per 0.5 µg selenium per gram hemoglobin ($p = 0.028$). The psychomotoric development of the girls improved by 12 points ($p = 0.002$). The authors concluded from this data that a lower prenatal selenium status is a disadvantage for the development of children.

Vanderlelie J, Perkins AV

Selenium and preeclampsia: a global perspective

Pregnancy Hypertens 2011; 1(3–4):213–224

This overview article compares the data on incidence of pre-eclampsia in almost 6.5 million births in 45 regions and matched them with their selenium status. Countries where the selenium level was at least 95 µg/l were thought to be sufficiently provided with selenium. The risk of pre-eclampsia was smaller. The incidence of pre-eclampsia was significantly lower in New Zealand and Finland, where there are government programs to ensure a better selenium supply.

www.ncbi.nlm.nih.gov/pubmed/26009029

Frequently asked questions

When is there a selenium deficiency?	The limit levels were specified by BfArM: a selenium deficiency is present at a selenium concentration of less than 80 µg/l selenium in the serum or less than 100 µg/l selenium in whole blood.
Why the active substance sodium selenite pentahydrate?	Only sodium selenite is approved as a drug. biosyn operates the first and until now only GMP manufacture of sodium selenite pentahydrate. The consumer can therefore rely on the safety and quality of selenase® products.
When can selenase® be obtained on a health insurance fund prescription?	The statutory health insurance providers must adopt the costs if a selenium deficiency has been determined before prescription.*
Can selenase® be taken with L-thyroxine or thyrostatic substances?	selenase® can be taken without problems with L-thyroxine or thyrostatic substances.
How long should selenase® be taken?	Therapy with selenase® for autoimmune thyroiditis is a long-term therapy. Upon discontinuation, the selenium status returns back to the original level within a few days.
What is the correct dose of selenase®?	The dose for autoimmune thyroiditis is 300 µg selenium per day.
Are there any adverse reactions?	No adverse reactions occur at a dose of 300 µg selenium per day.

* For German Health insurrance providers. On other cases contact your SHI Provider first.

Are there any interactions?

To date, there are no known interactions with other drug. The simultaneous intake of selenase® with food containing large quantities of Vitamin C should be avoided, since Vitamin C reacts with sodium selenite penthydrate to form elementary selenium, which the body cannot absorb. Wait about an hour after intake of Vitamin C to take selenium.

Can selenase® be taken during pregnancy?

Yes, selenase® can be taken without limitations during the pregnancy. A daily dose of 300 µg selenium is, according to EU, no reason for concern even for pregnant women.[84] Especially nursing mothers should ensure a sufficient selenium supply, since when breast feeding the mother requires 12.5 µg selenium more per day

selenase®

Active substance: Sodium selenite pentahydrate. **selenase® 100 µg pro injectione, selenase® T pro injectione, selenase® 100 µg peroral, selenase® T peroral, selenase® 50 peroral:** 50 µg selenium per ml. **selenase® 50 AP:** 50 µg selenium per tablet. **selenase® RP Tabletten:** 79 µg selenium per tablet. **selenase® 300 Mikrogramm Tabletten:** 300 µg selenium per tablet. **Indications: selenase® 100 µg pro injectione, selenase® T pro injectione, selenase® 100 µg peroral, selenase® T peroral:** Proven selenium deficiency that cannot be offset from food sources. Selenium deficiencies may occur as a result of states of maldigestion and malabsorption, as well as in malnutrition (e.g. due to complete parenteral nutrition). **selenase® 50 peroral, selenase® 50 AP, selenase® RP Tabletten:** Proven selenium deficiency that cannot be offset from food sources. Selenium deficiencies may occur as a result of states of maldigestion and malabsorption, as well as in malnutrition. **300 Mikrogramm Tabletten:** Adults: Treatment of clinically proven selenium deficiency that cannot be compensated by nutritional sources. **Composition: selenase® 100 µg pro injectione:** 1 ampoule of 2 ml solution for injection contains: 0.333 mg sodium selenite pentahydrate, corresponding to 100 µg (micrograms) selenium. **selenase® T pro injectione:** 1 injection vial of 10 ml / 20 ml solution for injection contains: 1.67 mg / 3.33 mg sodium selenite pentahydrate, corresponding to 500 µg / 1,000 µg (micrograms) selenium. **selenase® 100 µg peroral:** 1 drinking ampoule of 2 ml oral solution contains: 0.333 mg sodium selenite pentahydrate, corresponding to 100 µg (micrograms) selenium. **selenase® T peroral:** 1 ml oral solution contains: 0.167 mg sodium selenite pentahydrate, corresponding to 50 µg (micrograms) selenium. Excipients: Sodium chloride, hydrochloric acid, water for injections. **selenase® 50 peroral:** 1 drinking ampoule of 1 ml oral solution contains: 50 µg pure selenium as sodium selenite pentahydrate in a 0.9 % NaCl-solution. Excipients: Sodium chloride, hydrochloric acid, water for injections. **selenase® 50 AP:** 1 tablet contains 0.167 mg sodium selenite pentahydrate, corresponding to 50 µg (micrograms) selenium. Excipients: gelatin, magnesium stearate (Ph. Eur.), maize starch, sucrose, talcum. **selenase® 300 Mikrogramm Tabletten:** 1 tablet contains 300 µg selenium, corresponding to 0.999 mg sodium selenite pentahydrate. Excipients: Magnesium stearate (Ph. Eur., vegeatble), maize starch, povidone K25, sucrose, talc. **selenase® RP Tabletten:** 1 tablet contains 263 µg of sodium selenite pentahydrate, corresponding to 1 µmol = 79 µg (micrograms) of selenium. Excipients: Microcrystalline cellulose, sorbitol (Ph. Eur.), povidone K25, magnesium stearate (Ph. Eur.), palmitic and stearic acid. **Contra-indications:** Hypersensitivity to sodium selenite pentahydrate or to any of the excipients. Selenium poisoning. **Undesirable effects:** None known to date if the medicinal product is administered according to prescription. For **selenase® 100 µg pro injectione, selenase® T pro injectione:** *General disorders and administration site conditions:* Frequency not known (cannot be estimated from the available data): After intramuscular administration local pain at the site of administration has been reported. **Interactions: selenase® 300 Mikrogramm Tabletten** must not be taken together with reducing agents (e.g. vitamin C). However, selenase 300 Mikrogramm Tabletten and vitamin C may be administered consecutively with an interval of at least 1 hour between both administrations. **Form of administration, size of packages: selenase® 100 µg pro injectione:** 10 or 50 ampoules of 2 ml solution for injection. **selenase® T pro injectione:** 2 or 10 injection vials of 10 ml solution for injection, hospital-size pack 30 (3 × 10) or 50 (5 × 10) injection vials of 10 ml solution for injection, 2 or 10 injection vials of 20 ml solution for injection, hospital-size pack 30 (3 × 10) or 50 (5 × 10) injection vials of 20 ml solution for injection. **selenase® 100 µg peroral:** 20, 60, 90 or 100 ampoules of 2 ml oral solution. **selenase® T peroral:** 10 drinking bottles of 10 ml oral solution plus one measuring cup. **selenase® 50 peroral:** 50 drinking ampoules of 1 ml oral solution. **selenase® 50 AP:** 20 tablets, 50 tablets, 100 tablets. **selenase® RP Tabletten:** 50 tablets, 100 tablets. **selenase® 300 Mikrogramm Tabletten:** 20, 50, 100 tablets. **selenase® 100 µg pro injectione, selenase® T pro injectione, selenase® 100 µg peroral, selenase® T peroral, selenase® RP Tabletten, selenase® 300 Mikrogramm Tabletten:** **Subject to prescription. selenase® 50 peroral, selenase® 50 AP:** **OTC.**

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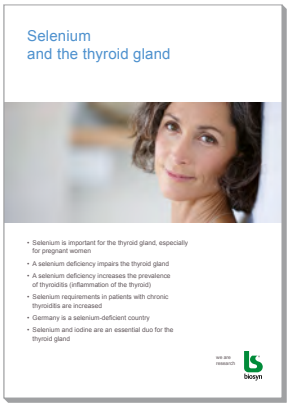

Selenium and
the thyroid gland
Folder for medical experts
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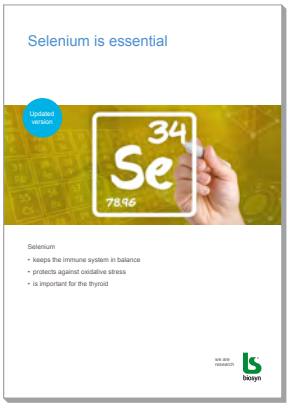

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biosyn Arzneimittel GmbH

World market leader in high-dose selenium injections

biosyn Arzneimittel GmbH is a pharmaceutical and biotech company based in Fellbach, Germany. It specializes in trace elements, is a world market leader for high-dose selenium injections, developer and operator of two unique GMP manufacturing operations for producing active ingredients, and in the biotech sector, is actively involved in the production of glycoprotein isolated from the Megathura crenulata, a sea snail found in California. 70 percent of our sales turnover is realized outside of Germany – in 26 countries all around the world.

With products developed for the areas of intensive care, oncology and endocrinology, biosyn is a partner to hospitals and physicians in private practice, as well as to naturopathic physicians and holistic health practitioners. We pursue research and development and evaluate the current medical-scientific literature as well as engage in modern online marketing. Our mid-sized family enterprise places great value on an open, engaged and customer-oriented corporate culture.


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Pregnancy, thyroid and selenium

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