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DISSERTATION

Titel der Dissertation

Selenium and immune mediated diseases of the thyroid

Verfasserin

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To my family and friends…

Erklärung

Ich erkläre des Eides statt, dass ich die vorliegende Doktorarbeit selbst verfasst und nur die angegebene Literatur verwendet habe.

Mag. Marianne Pestitschek

Wien, März 2011

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TABLE OF ABBREVIATIONS

AAS ……Atomic absorption spectroscopy

Ab ……antibody

AGES ……Austrian Health and Nutrition Safety Agency

AI ……Adequate Intake

AITD ……autoimmune thyroid diseases

ANOVA ……analysis of variance

As ……arsenic

BMR ..... Basal Metabolic Rate

BLS ..... Federal Food Key (Bundeslebensmittelschlüssel)

Bw …….. body weight

Cd ……cadmium

D_A_CH …….. Dietary reference values established between DGE, ÖGE, SVE

DGE …….. German Society of Nutrition e.V.

DHA ……Docosahexaenoic acid

DRI ……Dietary Reference Intakes

e.g. ……for example

EAR ……Estimated Average Requirement

EDTA .....Ethylenediamine tetraacetic acid

EFSA .....European Food Safety Authority

EPA ……Eicosapentaenoic acid

f……free (not bound, free in blood)

FFQ ……Food Frequency Questionnaire

FNA ……..fine needle aspiration

GPx ……glutathione peroxidase

Hg ……mercury

HT ……Hashimoto Thyroiditis

KES……..Kaiserin Elisabeth Hospital

kg .....kilogram

Lab..... Laboratory

MCT …….. medium-chain triglyceride

mm .....millimeters

OCP …… Oral Contraceptive Pill

ÖGE ……Austrian Society of Nutrition

Pb ……lead

PUFA ..... Polyunsatturated fatty acid

RDA …… Recommended daily allowances

SCF …… Scientific Committee on Food

SD ……..standard deviation

se ……selenium

SIS ……Selenium Intake Score

SIRS ……..Systemic inflammatory response syndrome

SGE/SVE …… Swiss Association of Nutrition

SPSS ……Statistical Package for Social Science

T_3 ……triiodothyronine

T_4 ……tetraiodothyronine/thyroxine

Tg …… thyreoglubuline

TPO ……thyroid peroxidase

TR ……..thioredoxin reductase

TRAK …… anti thyroid receptor antibody

TRH ……..thyrotropin-releasing hormone

TSH ……thyroid-stimulating hormone

TSIS ……..Total Selenium Intake Score

TWI ……...Tolerable Weekly Intake

UL ……Tolerable Upper Intake Level

USDA ……United States Department of Agriculture

vs. ……versus, contra, compared to

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I) INTRODUCTION

1.1. Facts and motives

According to the World Health Organization (WHO), chronic diseases like obesity, diabetes, and osteoporosis constitute the most frequent health problems in society. They are rapidly increasing. Also thyroid problems are common in many countries which in turn lead to a higher susceptibility to chronic diseases.

Steven Acuff reported in his lecture in October 2010 that nearly half of the population of industrialized countries suffers from thyroid dysfunctions, particularly from hypothyroidism, which make about 40% but also from hyperthyroidism at approximately 4% [ACUFF, 2010]. Every tenth citizen has the disposition to come down with an autoimmune mediated thyroiditis. Apart from that, the incidence of thyroid cancer has increased by 20% since the late 1990s, which is due to increased radiation exposure e.g. from x-rays [SHOMON, 2004].
The framework of the WHO International Programme on Health Effects of the Chernobyl Accident (IPHECA) and Chernobyl Sasakawa Project also showed a significant increase of the incidence of childhood thyroid diseases because of ionizing radiation [WHO, 2010]. Furthermore, about eight percent of the population suffers from goiter around the world [SHOMON, 2004].

About one-third of all human beings have to be medicated, but most of them do not know that they have thyroid diseases because the symptoms often are understated at the beginning. Symptoms are often very multifaceted, so that in a lot of cases they are not linked with thyroid. Thyroid is responsible for a lot of metabolism processes and that is why right diagnosis is very important. Too much or too little of thyroid hormones may totally unbalance a person’s body and psyche [MERCK, 2010].

Also in Austria, thyroid dysfunctions are among the most frequent diseases. Women are seven times more likely than men to develop thyroid disorders. The risk of thyroid disease increases with age, mainly above the age of 60 [SHOMON, 2004]. Also environmental contaminants interfere with thyroid function including 60% of all herbicides and heavy metals. Mercury, for instance, has antithyroid effects [ROMÁN, 2007]. But besides general living conditions and external influences, nutrition is one

of the most important factors relating to the development of a disease. Diet also influences the general state of health. As people hold the primary responsibility themselves for their own nutrition, the intake of the right foodstuffs is elementary.

As there is a lack of research relating to the thyroid gland and adequate nutrition, more research in this field has to be done.

1.2. Objectives of the study

As the thyroid has such a big influence on the total metabolism of human organism, disorders have to be counteracted as soon as possible. In accordance with literature and the newest research findings respectively one of the trigger factors of thyroid disease may be a selenium deficit [STOLL, 2010]. In Europe, selenium content in cultivatable soils is usually met within low ranges [SAGER, 2006]. Thus, according to Elmadfa and Burger (1998) the averaged daily selenium intake of the Austrian population is among the lowest worldwide. Although a lot of researchers are already concentrating on doing experiments with the trace element selenium and its relevance for thyroid, no special studies about thyroid health and diet are in existence.

From the 1970s onwards, it was recognized that an adequate selenium intake is necessary for immune processes [STREHL, 2006]. So, it received considerable attention for its antioxidant properties [BLEYS et al., 1993] and its important role in the immune system respectively. The significance of including adequate amounts of selenium in a person's diet is regarded as one of the most important discoveries in the last century [HATFIELD, 2001]. Selenium plays an important role in thyroid metabolism because of its participation in the iodine metabolism. Yet, there is need for more research.

Primarily, the aim of this study is to find out correlations between thyroid disease and diet but especially to find out if there is any relevance of the selenium status with regard to thyroid dysfunctions. The most interesting fact is the individual selenium intake by foods. It will be determined if selenium deficit influences thyroid function. Therefore, the Total Selenium Intake Score (TSIS) has to be calculated which will be compared with the blood Se levels to get information for detecting mistakes and short

comings in nutrition and showing differences when a sufficient selenium supply is granted. So, a FFQ has to be developed.
The significance of prophylaxis and the actual status of the selenium supply for thyroid patients will be analyzed carefully. Special nutritional patterns should be found and evaluated that may impair or improve thyroid function and selenium status. The intake of stimulants, the consumption of fruits and vegetables and the effect of physical exercises relating to thyroid function will also be examined. It will be particularly interesting to find out if nutritional habits may even influence special kinds of thyroid dysfunction like Hashimoto Thyroiditis or Morbus Basedow. So, individual nutrition or even diet mistakes of thyroid patients will be the most important target point of this study.

The increasing interest about the role of selenium in human nutrition led to the growing popularity of selenium-containing food supplements. Scientists see them as the best protection against civilization diseases [BIOSYN, 2010]. So, a lot of studies about selenium supplementation and thyroid function sustain the present research. And that is why even the effects of a selenium supplementation relating to thyroid function will be treated by means of case studies because supplements could not be given to the subjects.

Nutrition being a very important factor in the development and protection of all diseases, this study is meant to present very important background knowledge for people's health and their wellbeing.

"The selenium status of all populations should be known in order to take measures to alleviate a possible health risk that is easily corrected".

[GOLUBKINA and ALFTHAN, 2002]

II) LITERATURE SURVEY

2.1. The thyroid and its function

The thyroid is one of the most important organs of the human body. It regulates the oxygen uptake rate, the glucose, lipid, and protein metabolism and dominates the energy balance. Furthermore, it influences the thermal efficiency and the body temperature, the cardiovascular system, the gastrointestinal tract, the muscles and the nervous system. The thyroid also regulates the mineral and water balance and has influence on the human sex functions [LOHMANN, 2008]. Apart from that, the total physical and psychic development of children and adolescents depends on the thyroid function too. This all stresses the link between thyroid and nutrition.
The thyroid's anatomy and its functions have to be observed and understood as well before investigating the effects of nutritional habits. This will be described in the following chapters.

2.1.1. Anatomy of the thyroid gland

The healthy adult thyroid is the largest endocrine organ of the human and its average weight is about 20g [MEANS et. al., 1963]. Both its external structural construction and the macro- and microscopic anatomy, are very important for the comprehension of its functions [WISCHNEWSKI, 2005].
The thyroid (*Glandula thyroidea*) is a small butterfly-shaped gland and is located in the neck around the trachea. It consists of two lobes (*Lobus dexter* and *Lobus sinister*) which are connected with a cross-laying isthmus (*Isthmus glandulae thyroideae*) [WISCHNEWSKI, 2005]. The lateral lobes extend along either side of the larynx reaching the level of the middle of the thyroid cartilage. They usually measure from the superior to the inferior pole four centimeters, their breadth is 15-20mm, and their thickness ranges between 20 and 39mm. The gland is coated into the *Capsula glandulae thyroideae* which also consists of two parts; between them there is a movable disruption which is filled with a loosely connective tissue that explains the gland's mobility. The width and length of the isthmus is about 20mm, and its thickness is from two to six millimeters. The fibrous capsule, in which the thyroid is enveloped, sends septa into the gland's substance to produce an irregular,

incomplete lobulation. The shape and attachments of the organ are important for examination and diagnosis [MEANS et. al., 1963]. Figure 1 presents the macroscopic anatomy of the gland.

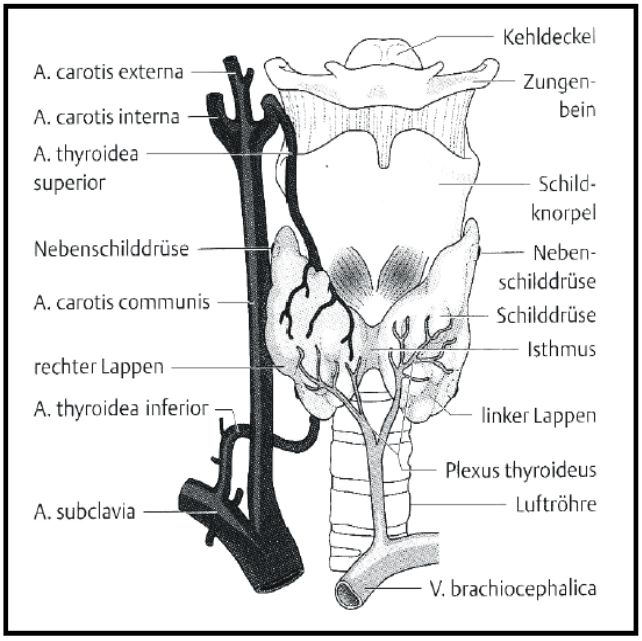


Figure 1: Anatomy of the thyroid [SCHWEGLER, 2002]

The thyroid has an abundant blood supply because its normal flow rate is about 5ml blood per gram thyroid per minute. So, the blood volume of normal men is about five liters which may be greatly increased in disease. The blood supply is provided with the four major thyroid arteries. The superior pair arises from the external carotid and enters the gland's substance. In contrast, the inferior pair arises from the thyrocervical trunk of the subclavian arteries, and enters the lower poles from behind. The fifth artery, the *thyreoidea ima* enters the thyroid in the midline from the arch of the aorta. There are free anastomoses between all these vessels. In addition, a large number of smaller arteriolar vessels derive from collaterals of the esophagus and the larynx supplies the posterior aspect of the thyroid. The branching of the large arteries takes place on the surface of the gland, where they form a network [MEANS et. al., 1963]. The venous blood is flowing off a venous network (*Plexus thyroideus*) which takes course before the trachea and ends into the *Vena brachiocepalica*. The thyroid hormones reside in the venous blood. These drain into the internal, the brachiocephalic, and occasionally into the anterior jugular veins [WISCHNEWSKI, 2005 and PFANNENSTIEL and SALLER, 1992].

The gland receives fibers from both sympathetic and parasympathetic divisions of the autonomic nervous system. The sympathetic fibers are derived from the cervical ganglions and enter the gland along the blood vessels. The parasympathetic fibers are derived from the vagus and reach the gland by branches of the laryngeal nerves. The fine structure of the thyroid cell is also very important because the acinar surface of thyroid parenchymal cells is covered with tiny villi. The colloid droplets are resorbed being prepared for secretion as hormones by the gland [MEANS et. al., 1963].

2.1.2. Thyroid hormones and iodine metabolism

Thyroid hormones provide for a good energy balance inside the whole organism. Its targeted production is closely adapted to the special need. There are four mechanisms that regulate the activity of the thyroid hormones, the extra-thyroidal metabolism, the neuro-endocrine regulation of the hypothalamus-pituitary-thyroid-axis but also the iodine supply by nutrition and the iodine balance [WISCHNEWSKI, 2005]. Some of the thyroid hormones' important effects of the body's metabolism are shown in Table 1.

Basal metabolic rate	- Elevated basal metabolic rate - Elevated oxygen uptake rate - Elevated warmth-production
Carbohydrate metabolism	- All metabolism-steps are elevated - Augmentation of the insulin-effect, -elimination and –supply
Lipid metabolism	- Augmentation of the lipid mobilization - Augmentation of reduction of fat storage - A little bit elevated lipid synthesis
Protein metabolism	- Physiologic dosages act anabol - Elevated hormone concentrations act catabol
Growth and development	- Length-growth: e.g. hormone deficit leads to nanism in adolescence - Brain development: irreversibly defects because of hormone deficit in fetal time (cretinism)
Bones metabolism	- Hormone excess may lead to osteoporosis
Musculature	- Changes of neuro-muscular transference (tendon reflex)
Cardiovascular system	- Augmentation of contractility and excitability of the myocardium - Augmentation of blood pressure amplitude, stoke volume and stroke frequency - Augmentation of the oxygen usage

Table 1: Important effects of the thyroid hormones [WISCHNEWSKI, 2005; modified]

The hypothalamus emits thyrotropin-releasing hormones (TRH) that tells the pituitary gland to produce thyroid stimulating hormones (TSH). TSH that circulates in the bloodstream is the messenger that stimulates the thyroid to produce the thyroid hormones T_4 and T_3 and then sends them into the bloodstream. When there are enough thyroid hormones the pituitary builds less TSH for slowing down hormone production. Thyroid problems can develop when something interferes with the system and the feedback process doesn't work any more [SHOMON, 2004]. By autoimmune thyroid diseases auto-antibodies can be built, which bind on the TSH-receptor and this can lead to stimulation (Morbus Basedow) or blocking (atrophic thyroiditis) of the thyroid function [WISCHNEWSKI, 2005]. The hypothalamic pituitary regulation and the exact way of the thyroid hormones are shown in Figure 2.

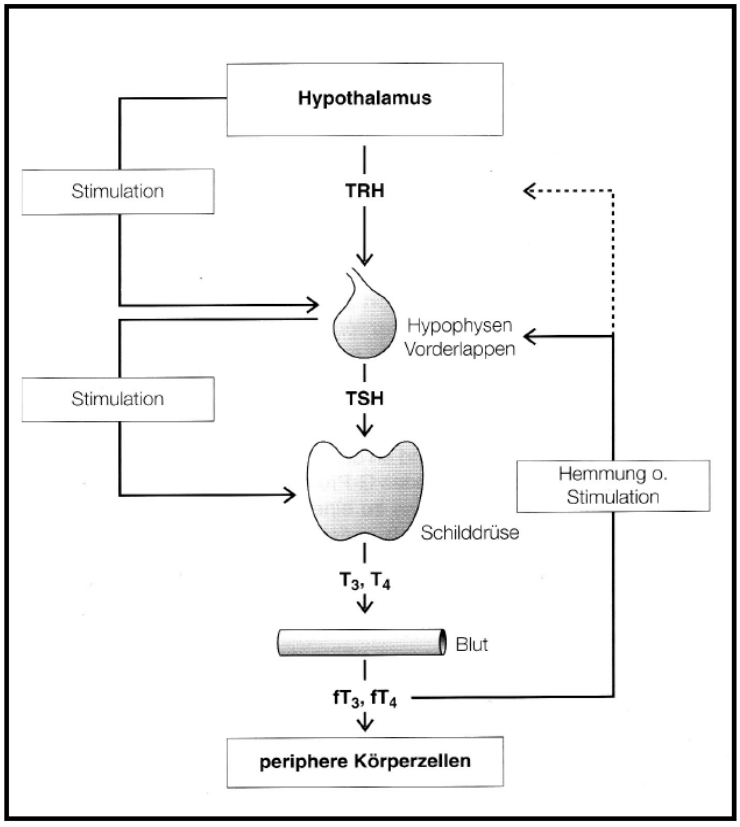


Figure 2: Hypothalamic pituitary regulation [PFANNENSTIEL and SALLER, 1992]

The thyroid function depends on the iodine supply and on the efficiency of the iodine metabolism. Generally, the thyroid needs iodine for the hormone production [MERCK, 2010]. Thyroid hormones and their precursors are the only iodine-containing compounds in the body with physiologic action. Rieger (2009) describes the thyroid hormones as the conversion of iodine in the “language” of the body. Thyroxine is 65% and triiodothyronine 58% of iodine by weight. For an adequate thyroxine synthesis, the thyroid has to absorb 60µg iodide daily. In blood iodine mainly appears bound as T_4, in small amounts as T_3 and as inorganically bound iodide [MEANS et. al., 1963 and ELMADFA and LEITZMANN, 1998]. With normal thyroid function about 80% become T_4 and 20% become the biological active hormone T_3. The rest of T_3 needed by the body is actually formed from the mostly inactive T_4 by a process sometimes referred to as T_4-to-T_3 conversion, which can take place e.g. in the thyroid, liver or in the brain [SHOMON, 2004].

Iodide gets absorbed via foods through the small intestine [MEANS et. al., 1963] and gets transported from the blood against a concentration gradient secondary-active through a sodium-iodide-symporter-protein into the epithelium cells of the thyroid [WISCHNEWSKI, 2005], where it filters out all the iodine. This is the so-called iodide transport which is presented in Figure 3.

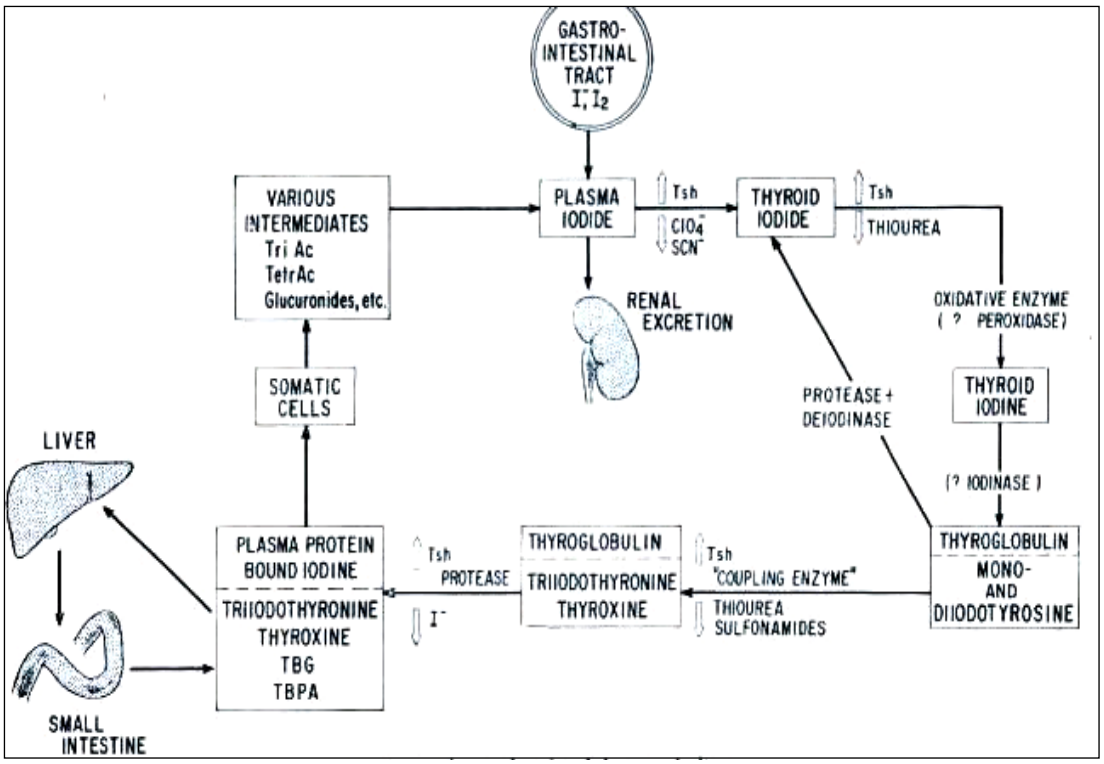


Figure 3: Iodine metabolism [MEANS et. al., 1963]

The adult thyroid gland is an agglomeration of follicles and here occurs hormone-containing secretion, called the colloid. It is a mixture of proteins, principally thyroglobulin, but also other iodoproteins and serum albumin. The follicles have no luminal connection with other parts of the body. Besides several other essential hormones, the thyroid's assignment is to build the two hormones tetraiodthyronine (T_4) and triiodthyronin (T_3) in the thyreocytes to tie them down to Tg. The thyroid releases T_3 and T_4 through the bloodstream to help cells converting oxygen and calories into energy [WISCHNEWSKI, 2005].

Plasma iodide that is transported into the thyroid cell is rapidly oxidized to elementary iodine or I_3^- and then bound to thyroglobulin (Tg). Here, it reacts with the tyrosine remain of the thyroglobuline to monoiodotyrosine (MIT) and diiodotyrosine (DIT)**.** MIT and DIT formed within thyroglobulin get deiodinated and are coupled to form thyroxine and triiodothyronine [WISCHNEWSKI, 2005].

The iodothyronines are the only known normal secretion products of the thyroid gland, which circulate in the plasma bound in dissociable linkage to several proteins.

The thyroxine-binding proteins serve to maintain a steady level of free thyroid hormone in the blood stream, and affect the rate of entry of thyroxine into the cells [MEANS et. al., 1963]. The two hormones, T_4 and T_3, are stored again as thyroglobulin (Tg) in the colloid of the thyroid follicles [WISCHNEWSKI, 2005] and after a variable period of storage it is cleaved, and the iodothyronines are liberated into the plasma. The thyroid hormones are transported into plasma attached by hydrogen bonds to proteins, and enter the cells of the body. There they exert their characteristic stimulatory effects on cell metabolism. The initial product is iodotyrosine [MEANS et. al., 1963 and ELMADFA and LEITZMANN, 1998]. In the connective tissue between the follicles there are C-cells, in which calcitonin is synthesized [WISCHNEWSKI, 2005 and MEANS et. al., 1963].

T_3 enters the cells via receptor sites on the cell-membrane and thus, cell metabolic rate increases, including body temperature. It also stimulates the cells to produce a number of different hormones, enzymes, neurotransmitters, and muscle tissue. The thyroid knows how much T_4 and T_3 to produce, because the release of hormones from the thyroid is part of a feedback process. The chemical formulas of the thyroid hormones are demonstrated in Figure 4.

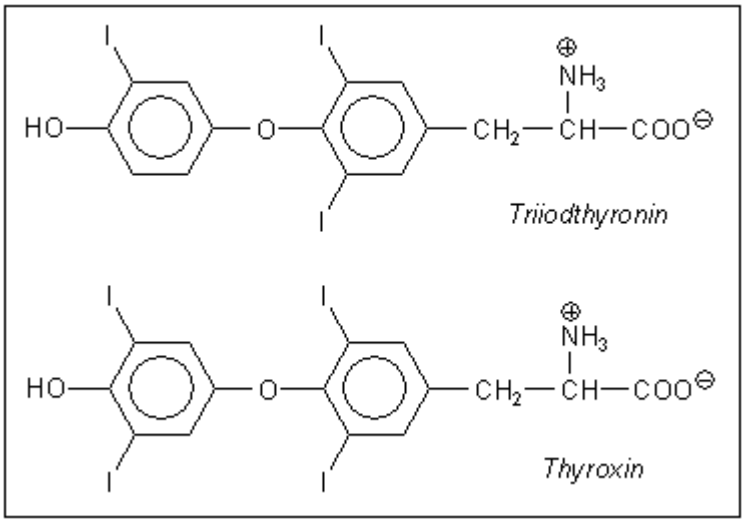


Figure 4: Thyroid hormones [BLUME, 2009]

The elimination of the thyroid hormones occurs for about 80% through stepwise enzymatic deiodination. Iodide that gets free during this process comes into the iodide pool of the body and stands by for the new thyroid hormone synthesis. The

remaining 20% of the thyroid hormones get degraded over other metabolic ways. One part even gets eliminated through the gall bladder [WISCHNEWSKI, 2005]. Renal clearance of iodide mainly is decreased in hypothyroidism, and increased in hyperthyroidism [MEANS et. al., 1963]. An iodine deficit augments the iodine concentration because then the iodine absorption of the gastrointestinal tract increases. More T_4 gets deiodized to T_3 and so, the synthesis of the biologic effectively T_3 gets augmented [WISCHNEWSKI, 2005]. Besides iodine, L-tyrosine is a known precursor to thyroid hormones too. Low tyrosine levels can make it difficult for the thyroid to function properly [SHOMON, 2004].

Generally, iodine and selenium are the most essential micronutrients for thyroid function. They are needed together and are required for thyroid hormone synthesis and function. Iodothyronine deiodinases are integral membrane proteins and each has a selenocysteine residue at the active centre that confers the high catalytic activity of the enzymes. They have different substrate specificities and tissue distributions and can catalyze the removal of iodine from the 5 or 5'positions of iodothyronine substrates [BECKETT and ARTHUR, 2005]. Three different selenium-dependent iodothyronine deiodinases (types I-III) can both activate and inactivate thyroid hormones [TRIGGIANI et al., 2009].

2.1.3. Thyroid function in pregnancy

Almost all kinds of thyroid diseases can appear in pregnancy. Thyroid hormones namely can cross the placenta. So, autoimmune thyroiditis is the most frequent cause of an initially diagnosed hypothyroidism and in pregnancy it often is transient and not often therapy obligatory. If the pregnant woman has a secure hypothyroidism thyroid hormones (T_4) are supplemented for protection of the fetus [WEISS, 2009].

Even if thyroid function is normal in pregnancy Postpartum Thyroiditis (PPT) can be developed which is a postpartal function disorder in the context of an autoimmune disease. Predictive factors are unknown type-1 diabetes, the age above 30 and an already appearing higher a-TPO-titer in the beginning of the pregnancy. Women with PPT have a significantly higher risk to develop hypothyroidism in the following ten years. By patients with known M. Basedow the TRAK-titer is determined in the third pregnancy trimester (22^{nd} to 26^{th} week of gestation). So, an accordant care of the

baby can be made in time. About 7% of all pregnancies are affected, but a high number of unreported cases are also guessed [WEISS, 2009].
The infant thyroid is hyperactive during the first weeks following birth. From the 10^{th} week of gestation even the thyroid of the fetus starts producing thyroid hormones. Mainly in the last trimester a thyroid augmentation may become noticeable. If there is a severe malnutrition pituitary function is depressed, and this also causes a fall in protein-bound iodine (PBI) but also a decrease in I^{131} uptake [MEANS et. al., 1963]. Often an already existing thyroid dysfunction only gets detected in the context of examination of the expectant mother. Here, a szintigraphy cannot be used for diagnosis because of adverse effects on the fetus [FRITZSCHE et al., 2004].

In thyrotoxic patients rates of abortion and miscarriage are slightly higher, and fertility is diminished. The thyroid gland typically undergoes hypertrophy during pregnancy, and the BMR is elevated. But pregnancy is also said to moderate the symptoms of thyrotoxicosis. Infants born of untreated thyrotoxic mothers or of mothers with well-controlled thyrotoxicosis may have typical signs of thyrotoxicosis with exophthalmos and goiter. If the mother is maintained in a euthyroid condition during the course of pregnancy, the child is normal at birth in all respects too [MEANS et. al., 1963].

2.2. Thyroid dysfunctions

Thyroid dysfunction is mainly induced by an autoimmune reaction of the thyroid or a chronic iodine deficit. According to the newest findings, a lowered defense against antioxidants is held responsible for auto-aggression because of selenium deficit [BOHNET, 2009]. The main conditions of thyroid dysfunction are shown in Table 2.

Dysfunction	Change	Description
Hypothyroidism	underactive thyroid	no production of sufficient hormones
Hyperthyroidism	overactive thyroid	too much production of hormones
Goiter	enlarged thyroid	can be found independent of thyroid function
Nodules	usually benign grown lumps	may cause hyperthyroidism (autonomous adenoma)
Thyroid cancer	malignant lumps or nodules in thyroid	
Postpartum Thyroiditis	temporarily inflamed thyroid	triggered autoimmunity after pregnancy

Table 2: Main conditions of thyroid dysfunction [SHOMON, 2004]

The autoimmune diseases Hashimoto Thyroiditis (HT) and Grave's disease are the most common causes of thyroid conditions. Here, the thyroid is targeted by the body's immune defenses as an invader [MEANS et. al., 1963].

Because the thyroid hormones relevantly affect the metabolism, thyroid dysfunctions have enormous consequences of the whole corporal and mental development, ability and psyche [MEANS et. al., 1963]. Every disorder of the thyroid hormone synthesis influences the basal metabolic rate [MERCK, 2009]. There is a strong connection between the function of the adrenal glands and the thyroid. An adrenal insufficiency can slow down overall metabolism and worsen thyroid problems [SHOMON, 2004].

2.2.1. Hashimoto Thyreoiditis and hypothyroidism

Hashimoto Thyroiditis (HT) is a form of the autoimmune thyroid disease (AITD). In HT immune system is fallen ill and not the thyroid because of an imbalance of the immune system. It can lead to hypo- and hyperthyreose with adequate symptoms [BRAKEBUSCH and HEUFELDER 2007 and WISCHNEWSKI, 2005].

Normally HT leads to hypothyroidism where the thyroid loses its ability to the synthesis of the thyroid hormones. Besides hypothyroidism, also the euthyroid state of the gland is possible. Mainly women are afflicted with chronic autoimmune thyroiditis. There are several explanations for the development of this disease, like immunotherapeutic agents or viral infections. Apart from the genetic predisposition, factors like neuroendocrine stress factors, high iodine doses, and abrupt hormone changes can affect the immune process too. Age, gender, or immune-stimulating

pharmaceuticals also are typical activators of Hashimoto Thyroiditis [WISCHNEWSKI, 2005]. The manifestation tops of HT lie peri-pubertal, -menopausal and postpartal [HEUFELDER, 2006]. Clinical manifestations of HT commonly include diffuse or nodular goiter with euthyroidism or sub-clinical and permanent hypothyroidism [MAZOKOPAKIS and CHATZIPAVLIDOU, 2007].

Two types of Hashimoto Thyroiditis are described in medical literature. The classic hypertrophic form is a diffuse painless and textural augmentation of the thyroid with possible advancing function loss (hypothyreotic struma). In such a case, a struma can be built which is linked with an iodine deficit disease; an enlargement of the thyroid is typically asymptomatic. Pain, tenderness or symptoms of thyrotoxicosis occur occasionally, and frequently, with time, hypothyroidism or full-blown myxedema develops. The diagnosis is suggested by the characteristic diffuse enlargement of the thyroid with involvement of the pyramidal lobe. The results of thyroid function tests are widely variable [MEANS et al., 1963]. The second type is the atrophic form of HT, which is a reduction of the organ's function because of a progressive inflammatory deletion of the thyroid tissue (primary myxedema). It may be slowly fractional or totally deleted [BRAUER et al., 2006]. The release of stored thyroid hormones causes transient thyrotoxicosis or hashitoxicosis [MAZOKOPAKIS and CHATZIPAVLIDOU, 2007].

Signs for diagnosis are the low basal body temperature [SHOMON, 2004] and high antibody titers. There are 90% antibodies against the thyroid peroxidase (a-TPO) and 60-70% antibodies against thyroglobuline (a-Tg). In sonography it is an echo-poor interior-structure of thyroid tissue [WISCHNEWSKI, 2005]. The characteristic Hashimoto Thyroiditis patient has high TSH values and usually low T_3 and T_4 thyroid hormone levels. Some patients have elevations in antibody levels for months or even years before an elevation of the TSH level [SHOMON, 2004]. Seldom can be found TSH-receptor antibodies (TSH-R-Ab), which lead to a slow deletion of the organ in an extreme situation [BRAKEBUSCH and HEUFELDER 2007 and WISCHNEWSKI, 2005]. This is the mentioned atrophic form of HT.

The therapy of hypofunction acts in accordance with the extent and cause of the disorder [BOHNET, 2009]. Generally, the treatment of hypothyreose by HT is with substitution of thyroid hormones (Levothyroxin) for the whole life [WISCHNEWSKI,

2005], in generally accepted usual replacement doses. But HT patients with a large goiter and normal or elevated serum TSH, L-T_4 may be given in doses sufficient to suppress serum TSH. Frequently, however, the disease is asymptomatic and no therapy is required [MEANS et. al., 1963]. Symptomatic patients with hashitoxicosis and low 24-hour thyroid radioactive iodine (^{123}I or ^{123}I) uptake (RIU) may be treated with beta-blockers (as propranolol) and sodium iodate or iopanoic acid (iodinated contrast agents) that block the peripheral conversion of T_4 to T_3 [MAZOKOPAKIS and CHATZIPAVLIDOU, 2007]. By an adequate therapy total recovery is possible [WISCHNEWSKI, 2005].

2.2.2. Morbus Basedow and hyperthyroidism

Morbus Basedow or Grave's disease is characterized in its classic form by hypertrophy and hyperplasia of the thyroid, hyperthyroidism (or thyrotoxicosis), and a unique type of ophthalmopathy. Generally, it speeds up the body's functions. Hyperthyroidism is caused by an excessive production of thyroid hormones. Thus, metabolism is distorted and accelerated in most tissues of the body. Hyperthyreosis may be caused exogenous, for instance by administration of thyroid or thyroid-stimulating hormones, or endogenous, induced by thyrotropin-secreting pituitary tumors [MEANS et. al., 1963].

A lot of metabolic abnormalities result directly from an excess of the thyroid hormones and elevated metabolic rate is conspicuous. The creatine metabolism changes to an increased excretion and lowered tolerance, the calcium metabolism shows an increased excretion (bone thinning), the cholesterol metabolism shows decreased concentration in the blood, and the carbohydrate metabolism changes to a depleted liver glycogen, decreased glucose tolerance, and often glycosuria. Morbus Basedow results as an unregulated, oligoclonal building of TSH receptor antibodies because of the unbalance of Th_1- and Th_2-cells and the B- and plasma-cell stimulation. In the thyroid this leads to a threocyte stimulation and hyperthyroidism and in the orbital tissues to a fat-cell recruiting. Grave's disease occurs at any age and is also more frequent in women [HEUFELDER, 2006]. A hereditary factor, emotional stress or trauma may be causes of Grave's disease [MEANS et. al., 1963].

The symptom pictures are dependent on hormone actions, personality, constitution, and reaction patterns of the subjects. There also are ophthalmologic features and localized myxedema. The entire nervous system shows hyperirritability, which is a major component in the functional disease process and symptoms. It causes accelerated heart rate and high blood pressure. Gastrointestinal motility is increased as well, which produces diarrhea. The striking changes in skeletal muscle, such as myasthenia gravis and actual atrophy, should be especially emphasized because they are less familiar than other signs [MEANS et. al., 1963].

Diagnosis usually is made by the TSH test because a low TSH level is an indicator. High levels of T_3 and T_4 are further indicators of hyperthyreosis. Additionally, thyroid-stimulating antibodies (TSAb) (or thyroid-stimulating immunoglobulin (TSI)) in blood are measured to diagnose Morbus Basedow [SHOMON, 2004]. The diagnosis of the classic form is easy and depends on the recognition of the main features of the disease and on confirmation by tests of BMR, PBI of blood, and collection of radioactive iodine by the thyroid. All these parameters are characteristically elevated in Graves's disease. Difficulties of diagnosis are to be found in the atypical cases. The physician has to include the different forms of therapy to the control of thyrotoxicosis but also the patient's psychic needs, the requirements for rest, nutrition, and specific antithyroid medications [MEANS et. al., 1963].

Grave's disease typically causes an overproduction of thyroid hormones, and if it is not treated it can become life-threatening. Morbus Basedow patients have to take antithyroid drugs and in case of recurrence a definitive treatment is recommended as therapy with radioactive iodine (131-I) or surgery (thyroidectomy). These patients become hypothyroid after an ablative treatment [SHOMON, 2004] and should undergo a substitution therapy.

2.2.3. Goiter

Generally, goiter (struma) can be developed in hyper- and hypothyroid states [SHOMON, 2004]. Often it is developed in adolescence as a general enlargement of the gland which produces pressure symptoms on the trachea or esophagus. It often represents the first stage of multinodular goiter formation [MEANS et. al., 1963]. Nodules can be solid or liquid filled and overactive where far too much thyroid hormones are produced. More than 90% of the nodules are benign, except among pregnant women, in whom about 27% of nodules typically are cancerous [SHOMON, 2004]. A colloid goiter is composed of uniformly distended follicles. If not caused by an autoimmune condition that triggers an inflamed thyroid, a goiter can come into existence due to the iodine level of the body. Struma stands in close relation to iodine deficit. An iodine deficit lowers the concentration of thyroid hormones in blood and the thyroid increases, because it tries to compensate the deficit of thyroid hormones with a higher production output [HAMM, 2006 and LEITZMANN and DITTRICH, 2003]. Generally, iodide deficiency, dietary goitrogens, enzymatic defects in hormone synthesis, or a combination of these factors may cause the thyroid to grow and gradually evolve into an organ containing hyperplastic islands of normal glandular elements, together with nodules and cysts of varied histological patterns [MEANS et. al., 1963].

Symptoms of thyroid nodules include palpitations, insomnia, weight loss, anxiety and tremors, which are all common in hyperthyroidism. Nodules also can trigger hypothyroidism and symptoms often include weight gain, fatigue, and depression. Some people vary between hyperthyroid and hypothyroid symptoms. Others have difficulty swallowing, feelings of fullness, pain, or pressure in the neck, a hoarse voice, and neck tenderness. But there are also people who do not have any obvious symptoms related to thyroid dysfunctions at all [SHOMON, 2004].

For therapy also thyroid hormone replacement-drugs are given that help to shrink. Treatment of goiter mainly depends on how enlarged the thyroid has become [SHOMON, 2004]. Nodules should be monitored periodically to attest that they are not causing serious difficulties. The toxic nodular goiter is treated with radioactive iodine. Thus, a reduction of the goiter size and control of the thyrotoxicosis is expected [MEANS et. al., 1963].

2.2.4. Thyroid cancer and Thyroiditis de Quervain

The number of thyroid cancer cases is on the rise although it is a fairly uncommon cancer. In contrast to other thyroid diseases, men are affected more frequently by it than women. Papillary and follicular thyroid cancers are the most common types. But also medullar thyroid cancer that is split into the sporadic and familial form occurs. People with a family history of medullar thyroid carcinoma (MTC) have to make a blood test of the calcitonin levels, which indicates a strong possibility of a genetic predisposition. Then a thyroidectomy is performed as a preventive measure [SHOMON, 2004].

Treatment and prognosis of thyroid cancer depends on its type. The main diagnostic procedure of suspected cancer is the fine needle aspiration (FNA) biopsy of the nodule. Here, fluid and cells are removed from various parts of all nodules and then evaluated. If a case is classified as suspicious, a surgical biopsy is necessary. With the exception of pregnant women, everybody has to have a radioactive thyroid scan in order to identify if the nodules are “cold”, which means that there is a greater cancerous potential. Most of thyroid cancers are treated successfully when discovered early [SHOMON, 2004].

Another but rather unusual form of thyroid dysfunction is *subacute Thyroiditis de Quervain*. It is named after *Fritz de Quervain* who first described this disease. In dated back studies there could be determined a recently preceding infection of the upper respiratory tract. It often appears some weeks after a virus infection, mainly an infection of the upper air paths. But it is not definitely proven that the infection is caused by a virus. This inflammation is very painful and sometimes accompanied by struma. Patients suffer from general symptoms like fever and abnormal fatigue and are treated with anti-inflammatory drugs. A therapy with cortisone preparations eliminates the symptoms within some hours [PFANNENSTIEL and SALLER, 1992 and MERCK, 2009].

2.3. Nutrition and thyroid

By controlling the energy production and oxygen ingestion, the thyroid rules the whole metabolism. It influences particularly the gastrointestinal tract and functions as a regulator of the glucose, lipid, and protein metabolism. The thyroid also regulates the mineral- and water balance of the body and that is why it shows a big coherence to nutrition [MCKEITH, 2005]. This makes it clear that thyroid problems can be enhanced by a change of the usual nutritional habits [ACUFF, 2010]. Nutritional deficiencies, toxins and a variety of other physiological factors prevent the body from accomplishing that conversion process from T_4 to T_3 properly and so a T_3-deficiency occurs [ACUFF, 2004].

2.3.1. Main nutrients and thyroid function

Proteins are composed of amino acids. They are differentiated into essential (*isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan,* and *valine*) and not-essential amino acids (*alanine, asparagine, aspartic acid, glutamine, glutamic acid, glycine, proline,* and *serine*). Proteins exercise a very important protective and defense function, for instance as antibodies (immunoglobulins) and as different coagulation factors (fibrinogen and thrombin). As plasma proteins act as transport proteins too, selenium gets bound on plasma proteins into blood. Therefore a protein-rich nutrition is very important because Se only appears in connection with proteins [ÖGE, 2010]. The most important function of proteins is their function as enzymes and some hormones also contain protein or amino acid components. The thyroid combines iodine with the amino acid tyrosine and then, converts the iodine/tyrosine combination into the hormones trijodothyronine (T_3) and thyroxine (T_4). For the synthesis of tyrosine phenylalanine is essential for the thyroid because it provides the benzene ring which is important for the hormone synthesis. Phenylalanine has to be absorbed by nutrition. Only from phenylalanine tyrosine can be built and not the other way round. Thus, phenylalanine is essential and tyrosine conditionally is essential. Tyrosine plays an important role in the synthesis of the thyroid hormones T_3 and T_4 [ELMADFA and LEITZMANN, 1998]. If there is a deficiency, the production of tyrosine is not possible anymore and tyrosine gets essential. In stress situations the demand of tyrosine increases [STRAUSS, 2008]. Generally, phenylalanine and tyrosine are contained in milk and its products, meat and pulses, like lentils, peas, beans [KIEFER and ZIFKO, 2007]. The only tyrosine-

containing foods are pumpkinseeds, avocados, almonds, and fish [MCKEITH, 2005]. If a person consumes a lot of organic iodine and tyrosine, it leads to a better iodine absorption and utilization [RIEGER, 2009].

The synthesis from phenylalanine to tyrosine is demonstrated in Figure 5.

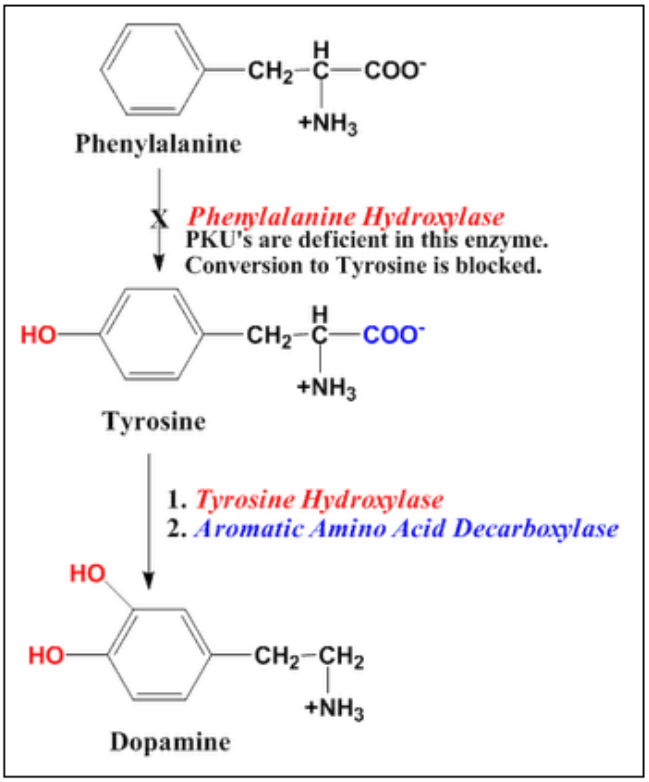


Figure 5: Change from phenylalanine to tyrosine [IVERSON, 2009]

The second main nutrients are dietary fats. They additionally have to be mentioned because selenium also affects the lipid metabolism [THOMSON, 2004]. The amount and composition of nutritional fats play an important role. The right proportion of saturated and unsaturated fatty acids (1:5 or 1:3) has positive effects on the immune system and thus, boosts thyroid health. Polyunsaturated fatty acids (PUFA) are immune active substances and have positive effects on the metabolism, microcirculation and inflammation reactions. So, a high alimentary intake of PUFAs is advised [SCHÄFER, 2003]. Anti-inflammatory measures advise the consumption of fewer animal fats and at the same time more omega-3-fatty and gamma-linolenic acids [HEUFELDER, 2006]. Fish oil, krill-, and liver oil are the best omega-3 sources, especially for hyperthyroid patients. But according to the presentation by Steven Acuff in October 2010 polyunsaturated fatty acids also have to be consumed in

moderate amounts [ACUFF, 2010]. Acuff recommends coconut oil, which also consists of about 92% of saturated fatty acids. But most of those are medium-chained and that is why their metabolism is different to those of animal origin. Medium-chained fatty acids do not undergo degradation and re-esterification processes and are directly used for energy production in the body. This makes them significant dietary fats [AMARASIRI and DISSANAYAKE, 2006]. Furthermore, according to the National Nutrient Database for Standard Reference (USDA), coconut oil contains very high amounts of lauric acids, which have a supporting effect on the thyroid. Thus, coconut fats are very helpful with thyroid problems. For instance, Gupta et al. (2009) found that rabbits fed on soybean oil had a significant increase in TSH levels and gained more weight when compared to rabbits fed on coconut oil [GUPTA et al., 2009]. This shows the positive effect of coconut oil on the thyroid although it is not known in how far animal trial tests relate to human metabolism. Fish is also a very important source of dietary fats. Domestic kinds of fish like salmon, Atlantic herring, sardines, mackerels, and coalfish are qualified for regular consumption and they, each in a different way, add to the optimal intake of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) [WIDHALM et al., 2007].

Carbohydrates compose the third main nutrient group that play an important role in thyroid health. Some thyroid patients are carbohydrate sensitive and can only lose weight by strictly limiting starchy foods. Hypothyroidism lowers – besides all metabolic ways of the organism - the carbohydrate converting and at the same time the ability for blood glucose absorption of the cells decreases. Carbohydrates proliferate to such an extent that excessive insulin is produced, which in turn causes weight gain. Hyperthyroid patients should also take care of the consumed amounts and kinds of carbohydrates; especially foods with high GI should be avoided. Generally, a balanced approach to e.g. proteins, starches, vegetables, fruits and fat is needed [SHOMON, 2002 and SHOMON, 2004].

2.3.2. Iodine in foods and its significance for thyroid

Iodine is the most important essential trace element that has to be mentioned with reference to the thyroid. Iodine affects the thyroid function and is used for the thyroid hormone synthesis [POLUNIN, 2008]. It has to be absorbed with nutrition and drinking water. Iodine mainly appears as inorganic iodide and in this form it gets

almost completely absorbed [ELMADFA and LEITZMANN, 1998]. Two-thirds of the absorbed iodine is excreted by the kidneys, and about one-third is accumulated by the thyroid gland [MEANS et. al., 1963]. Table 3 shows the exact iodine supply of different age-groups.

Age groups	**Iodine need (µg/ day)**
Infants up to 4 months	50
Infants from 4-12 months	80
Children from 1-7 years	100-150
Schoolchildren from 8-13 years	180
Adolescents and adults from 14-50 years	200
Adults from 51 and older people	180
Pregnant and breast-feeding women	230-260

Table 3: Daily iodine need of different age groups [MERCK, 2010]

Although, since 1963, iodine has been added to table salt, which showed an augmentation in iodine accumulation, iodine deficiency still exists [MERCK, 2010]. In Austria, iodine is supplemented with 20mg potassium iodide or -iodate per kg table salt [AGES, 2005]. Without iodized salt average nutrition would lead to the gland's hypofunction [HEUFELDER and BRAKEBUSCH, 2007]. According to Dickau (2009), the use of iodized table salt does not show any danger for iodine oversupply. But according to Rollinger (2010) the most important question is about the iodine-overdosage and the consequences for health because in nearly all foods people are faced with iodine supplementation: iodinated animal foodstuffs with high iodine contents in animal products, iodized salt in food production and even iodized salt in the local cuisine [ROLLINGER, 2010]. Even multi-vitamin preparations, drugs supporting the thyroid function and other active components contain iodine [SHOMON, 2002]. More than 1000µg are dangerous for people with a mild thyroid hyperfunction, which might consequently change into a heavy progressive form and HT might worsen. Attention should also be paid to the ingredient lists of foods because only by doing this consumers can find out if added iodine is contained or if it is not [HEUFELDER and BRAKEBUSCH, 2007]. Hence, iodine sensitive people have to avoid convenience foods.

The main natural sources of iodine are fish and seafood, especially crustaceans [POLUNIN, 2008]. 1-2 times seafish should be eaten weekly for optimal iodine absorption [DICKAU, 2009]. Table 4 shows the iodine contents of different foods listed from the highest to the lowest iodine content.

Sea fish (µg/100g)		**Other foods (µg/100g)**		**Other foods (µg/100g)**	
Haddock	243	Iodized salt	2000.0	Broccoli, cooked	14.9
Codfish	130	Gervais (55%fat)	40.0	Peanuts, roasted	14.0
Mussels	170	Emmental (45%)	40.0	Sunflower-seeds	14.0
Redfish	99.0	Parmesan	40.0	Cow-liver	13.0
Plaice	53	Lettuce	35.0	Spinach	12
Herring	52	Cow/calf-heart	30.0	Chicken-egg	10
Halibut	52.0	Brie (70% fat)	20.0	Rye bread	8.5
Mackerel	48.0	Camembert (60%)	20.0	Radish	8
Tuna	50	White mushrooms	18.0	Lamb	5
Salmon	34	Mozzarella	15.0	Edam-cheese (45%)	4
Sardines	32.0	Parsley	15.0	Cow-milk	3.3
Kipper	31.0	Carrots	15.0		

Table 4: Iodine content of different foods [KIEFER and KUNZE, 2008 and MERCK, 2010; modified]

Generally people with hyperfunction should avoid iodine-rich foods till hyperfunction has been treated and the thyroid function is normal again [MERCK, 2010]. Rieger (2007) advises people with hypofunction to eat coalfish or algae daily. But people have to be well schooled in the consumption of algae. Two to three teaspoons of blue-green algae meet the demand of the iodine supply (1 teaspoon= 80µg iodine). [AGES, 2010].

2.3.3. Substances and thyroid

Both, with hypo- and hyperfunction the absorption of all nutrients is impaired. Iron, for instance, is an important component of the thyroid enzyme TPO [HESS, 2003]. Zinc helps - along with selenium - to prevent the decline of T_3 when a person is on a low calorie diet. When there is a selenium deficiency the high intake of iodine generates thyroid damage [SHOMON, 2004].

A lot of nutrients can affect the thyroid function negatively [HESS, 2003]. The thyroid may be sensitive to nearby metals from the periodic table like silver, tin, cadmium, barium, or caesium, which are very toxic in high doses. Further harmful substances that disrupt the iodine absorption are humic acid in the ground water, dioxin, polychlorinated biphenyl (PCB) and thiocyanates from cigarette smoke [RIEGER, 2009]. A copper-zinc imbalance can impede conversion of T_4 to T_3, even in people whose thyroid hormone levels are normal. So, foods with high copper levels but also foods and drinks that deplete zinc like alcohol, coffee, sugar, and excessive carbohydrates should be avoided [SHOMON, 2004]. Fluorine and chlorine - contained in drinking water and fluorine additionally in toothpaste – also seem to disturb the optimal conversion of the thyroid hormones, which leads to hypothyroidism [MEANS et. al., 1963]. In contrast, fluoride is used in the treatment of hyperthyroidism, because it suppresses the thyroid function [SHOMON, 2004]. Mercury exposure that comes through dental fillings and fish is able to disrupt the conversion from T_4 to T_3. So, it leads to hypothyroidism [SHOMON, 2002]. Also calcium has goitrogenic effects when it is absorbed in excessive amounts. It may also lead to a borderline dietary iodine deficiency. Furthermore, nitrate, bromide, and cobalt also have antithyroid activity but they are of little significance in the goiter production of men [MEANS et. al., 1963]. Solanine-containing foods *(Solanaceae)* like potatoes, tomatoes and aubergines are very important in relation to thyroid. Especially potatoes represent the basis of Austrian meals. Solanaceae namely contain solanine that blocks the cholinesterase, which may lead to inflammations [ACUFF, 2010].

Vitamin deficits should be eliminated before thyroid dysfunction is treated. If there are latent nutrition or digestion problems thyroid hormones namely cannot be absorbed in the right way and so the body cannot use them. Some forms of hypothyroidism actually reflect nutrition deficits and if this is the case, thyroid function can be rebuilt again. Achieving a balanced TSH level is difficult. L-tyrosine is advised because low concentrations of it appear in connection with hypothyroidism. Besides iodine and selenium, even B vitamins are very important for thyroid health because sugar consumption leads to the resorption of B vitamins. Vitamin B_1 and B_2 are absolutely important for general health in hypothyroidism because both intrinsically are tied to energy metabolism which regulates thyroid. Furthermore, vitamin B_1 is important for

carbohydrate metabolism. Vitamin B_2 is part of the thyroid metabolism because it affects as catalysator by deiodination of T_4 to T_3 [SHOMON, 2002]. Vitamin B is to be found in foods with lactic acid fermentation like *sauerkraut* or brown rice [ACUFF, 2010] but also in meat and dairy products. Furthermore, vitamin B_2 and yeast, vitamin C, vitamin E and zinc are important for immune and thyroid function too. Fish is a further donor of proteins, vitamins (D and B_{12}) and fats. Besides fish, egg yolk also is a secure source of vitamin B_{12} [ACUFF, 2004].

Nutrient supplementation has also to be mentioned concerning the thyroid. Only if there is a deficit of vitamin C or E, these nutrients should be supplemented as soon as possible because thyroid cells rapidly grow by this stress. If there is a thyroid hypofunction β-carotin cannot be changed into vitamin A, which is an indicator of an asthenic thyroid. Bio-butter, for instance, is high in vitamin A. Generally, the thyroid also needs the other fat-soluble vitamins: vitamin D, E, and K [SHOMON, 2002].

2.4. Overview of the trace element selenium

In the earth's crust selenium appears among the sixty most frequent elements. Selenium is contained only in trace concentrations like 50-200µg/kg, but in some minerals it is highly enriched [SIMONOVA and PFANNHAUSER, 2008]. Selenium is mainly concentrated in sulfidic ores because it is able to socialize with sulfur. There are big variations possible, because the sulfur ores appear in very irregular spreading on the earth's surface [UNTERWEGER, 2001]. As of the similar structure, it also develops instead of sulfur into methionine and cysteine in the organism [UNTERWEGER, 2001 and ELMADFA and LEITZMANN, 1998]. It appears in sulfides or in living and dead organisms [SAGER, 2005].

Compared to several other elements of nutritional importance, selenium still is a relatively little understood food component [SIMONOVA and PFANNHAUSER, 2008]. It is the primary source of metals and metalloids in foods [UNTERWEGER, 2001]. Selenium was discovered in 1817 by the Swedish scientist Jöns Jacob Berzelius. At that time selenium was known as a toxic mineral and it needed a further 140 years until its nutritional essentiality for humans was proved [STOJANOVIC, 2000 and SAGER, 2006]. In 1973, Flohe et al. (Germany), and Rotruck et al. (USA), demonstrated that selenium is an integral compound of the glutathione peroxidase (GPx) of different animal species. Finally, in 1975, Awashti et al. detected selenium in

the GPx of humans [ELMADFA and LEITZMANN, 1998]. In Europe, the main problem is how to ensure sufficient selenium supply in human nutrition [SAGER, 2006].

Selenium acts in biophil and chalkophil ways [SAGER, 2005]. Selenium is placed in the group VI-A of the periodic system, between sulfur and tellurium and has six stable isotopes and several allotropic forms in the solid state. The structure of selenium depends on pressure and temperature, and on the composition of impurities [CIZIKOV, 1968]. Selenium is incorporated into proteins as selenocysteine, which is the 21st naturally occurring amino acid in proteins [HATFIELD, 2001].

2.4.1. Selenium spreading on earth and sources

The biggest part of the earth does not contain a lot of selenium and this explains why Se deficiency appears more often than the excess of it [WISCHNEWSKI, 2005]. Generally, two selenium-poor zones on earth are described. The southern hemisphere includes the total European area, parts of the former Soviet Union, China and New Zealand [STÜCKLER et al., 2010]. In China, for example, deficiency regions have about 0.09-0.17mg/kg and toxicity regions more than 1.70mg/kg selenium in their soils [SAGER, 2006]. High selenium concentrations have been detected in the western states of the USA, parts of China, Russia, and Venezuela [WISCHNEWSKI, 2005].

People's environment is the primary source of all the selenium absorbed through foods and beverages. Selenium is probably ubiquitous because it occurs in all soils [REILLY, 1996]. Selenium concentrations considerably vary in soils, because of the regional differences of its contents in cultivated plants and animal organisms [ELMADFA and LEITZMANN, 1998]. A variety of factors control the level and the form of selenium at the beginning of the food chain. Selenium has its seeds in soil or soil-applied emissions and is absorbed by plants from the atmosphere and utilized by farm animals and humans [REILLY, 1996]. The following graphic, Figure 6, presents the environment's selenium cycle.

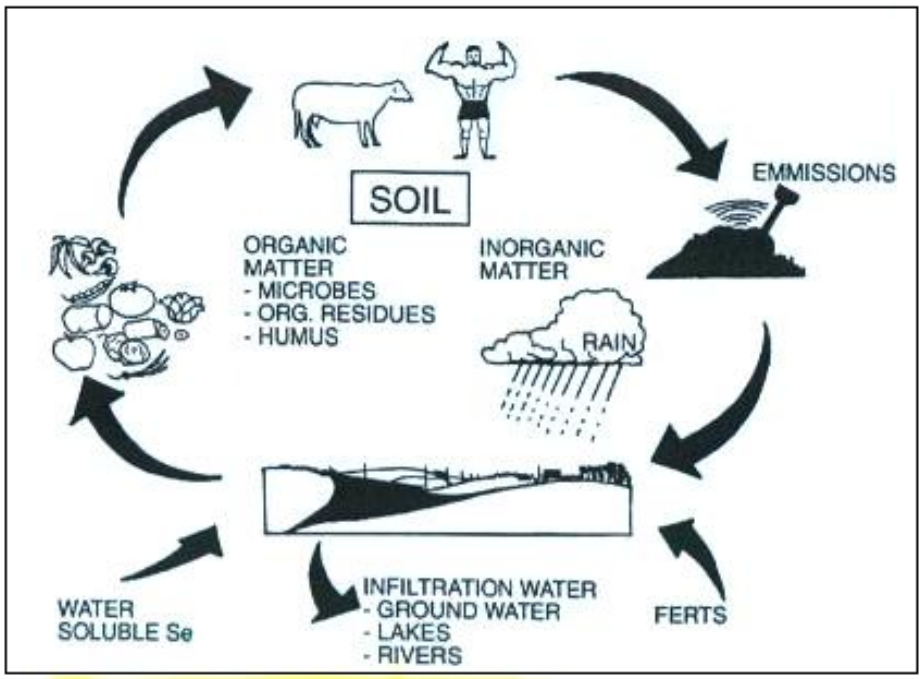


Figure 6: Selenium cycle [REILLY, 1996]

Apart from industrial and mining activities, the main selenium sources are the burning of coal and the selenite additions to animal feedstuffs. In soils and crops, selenium levels get enhanced by the recycling of manure, dung, and sewage sludge, which is beneficial for Europe. Reduction processes in sediments, soils, and feedstuffs act as sinks for available selenium forms [SAGER, 2006].

According to the WHO, drinking water only makes a small contribution to the selenium intake [REILLY, 1996]. In natural and domestic waters its concentrations are generally very low [SAGER, 2005]. The selenium content of natural waters can vary within a broad range, from less than 2ng up to 300µg/l. In Austria the upper tolerance limit is 10µg/l for use as potable water (Austrian Federal Law: BGBl 1995/359) but – as already mentioned - it is hardly reached [SAGER, 2006].

2.4.1.1. Selenium occurrence in soils and absorption of plants

The selenium level of soils depends on geochemical factors, especially on the nature of the prehistoric rock. Natural and human activities also play their part in determining how a soil fits into the selenium rating scale [REILLY, 1996]. There are no significant differences between soils on diverse geological underlayers and in soil profiles of the alpine grassland [SAGER, 2005].

Besides the total selenium concentrations, both, the chemical form and various environmental factors, determine the plant's availability of the element. In alkaline, well ventilated soils selenium mainly appears as selenate, which is well available for plants. Selenites represent the most important Se sources but under acid conditions, selenite tends to bind tightly to clay particles and iron complexes. Thus, its availability is reduced [REILLY, 1996]. In contrast, hardly soluble selenides and elementary selenium from acid and wet soils are of little use. The so-called acid rain, through the lasting accumulation of the soils with sulfur and its natural antagonism to selenium, leads to a reduction of the bioavailability in the food chain [ELMADFA and LEITZMANN, 1998]. Low selenium contents in soils and reductive ratios like high rainfalls, for example, are the typical situations in the alpine area and in the *Böhmische Masse,* including Austria, Bavaria, Czech and Slovakia [STÜCKLER et al., 2008]. The antagonistic interactions between selenium and heavy metals are part of its function [ELMADFA and LEITZMANN, 1998]. So, the primary selenium forms include selenate, selenite, elemental and organic selenium [CAI, 2003]. Selenates can pass over to drinking water too [UNTERWEGER, 2001 and ELMADFA and LEITZMANN, 1998].

The tendency of plants to accumulate se, partially corresponds with their sulfur requirement. Plants that normally are rich in sulfur, such as members of the *Liliaceae* family (onions and garlic) and members of the *Cruciferae* family (including cabbage and broccoli) are rich in selenium. Even on seleniferous soils, not all crops take up toxic levels of the element [REILLY, 1996]. Leaves and kernels usually have higher Se contents than roots and stalks. Green plants like vegetables accept sodium-selenate more readily than selenite from soil solution [SAGER, 2005].

Absorption of elements in aqueous solution through the roots from the surrounding soil is the main route of entry, under neutral, oxidizing and low-carbon conditions. Amino acids, selenite and selenate can directly pass into plant roots [SAGER, 2005]. The amount of an element taken up by the roots largely depends on its soil solution concentration, although its chemical form, the presence of other elements and e.g. the plant species are also crucial factors. The season of the year can also affect the uptake. While higher plants are the primary distributors of Se from soil to foods, they themselves do not appear to require it for their own metabolism. Lower plants, such as algae, require selenium for growth [REILLY, 1996].

Selenium-binding proteins like selenomethionine are synthesized by plants and microorganisms. This is the principal form of selenium that occurs in cereals and other plant foodstuffs. Selenomethionine can be converted into selenocysteine by the trans-sulfuration-enzymatic-pathway; it cannot be directly used for the selenoprotein synthesis and so, first has to be changed into other forms [REILLY, 1996].

The Se content of flora significantly varies with the geological origin of soil, pH, plant species and age, as well as with the protein content of the consumed plant parts. Intense fertilization with mineral fertilizers, lead to a decline of Se levels in the crops because of dilution effects. In Central Europe, the flora grown on neutral loess soils contain more Se than grown on acidic soils [STÜCKLER et al., 2010 and ANKE et al., 2002]. Within the Austrian soil-monitoring program, median values of total selenium for various soil types ranged between 0.11-0.41mg/kg for total selenium, irrespective of the geological facies below [SAGER, 2006]. But generally, by long-lasting intensive utilization of farmlands an added selenium loss appears [SIMONOVA and PFANNHAUSER, 2008]. The main entry sources of Se in Austrian soils is the slurry from intensive pig breeding [SAGER, 2005]. The heigh of the selenium content of stable manure or slurry depends on the used supplementary feedingstuff by the single animal categories [HOESCH, 2010].

2.4.1.2. Selenium donation in feedingstuffs and fertilization

If the natural nutrient contents of agricultural products are not enough, they often have to be added. In the 1980ies, selenium first was added to commercial feedingstuffs [SAGER, 2006]. In many parts of the world, selenium is used as a nutritional supplement in animal agriculture [STOJANOVIC, 2000], which generally increases selenium status. In Austria, too, the supplementation of feedingstuffs of agricultural productive livestocks with the essential trace element selenium has been practiced for some years. But feeding practices are not easily traceable to products sold in the market [SAGER, 2006]. In hog feeding and poultry mast the se-rich imported feedingstuff soy extraction pellets are used. This explains why especially these kinds of meat have high Se contents [STÜCKLER et al, 2010]. Figure 7 presents where selenium is added to foodstuffs of different animal species.

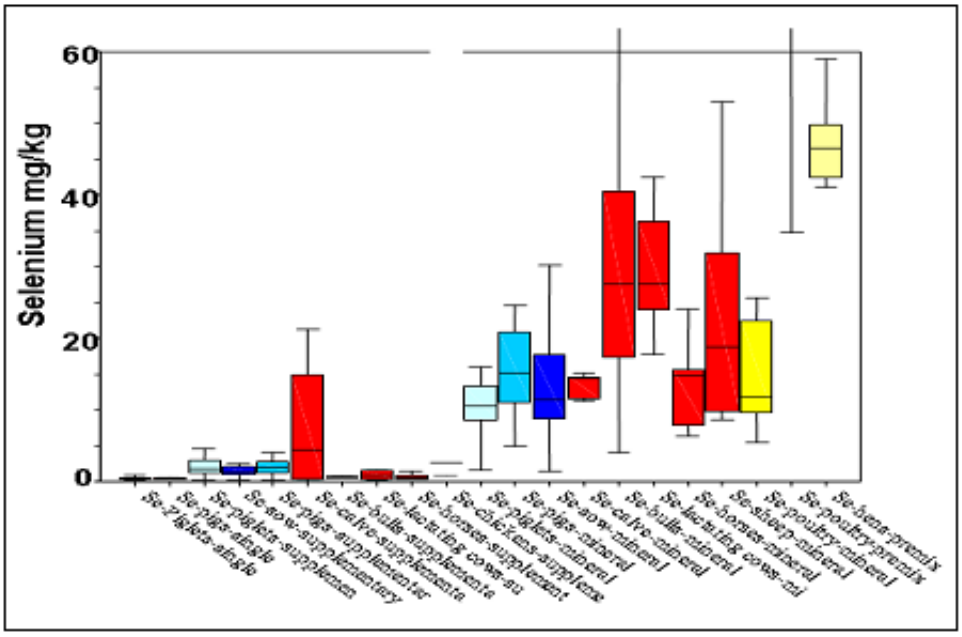


Figure 7: Selenium in animal feed [SAGER and LAGUNA-PAREDES, 2010]

Commercial animal fodder usually contains added sodium-selenite or -selenate. But organic compounds that are usually contained in foods and living biota, like ascorbic acid and oxalate, can gradually reduce major parts of added selenite, presumably to elementary selenium [SAGER, 2006]. In a pilot study from *Graz* and the surrounding areas Se was determined in some samples of meat, liver and kidneys. The higher Se contents of pork resulted from enriched animal feed and from better resorption [STÜCKLER et al, 2010]. In contrast to that, ruminant animals have lower levels because selenium gets reduced and lost by the microbial flora in the forestomachs. Differences in the selenium contents of beef and veal are explained by different feeding habits. Fish muscle contains about double Se of meat [SAGER, 2006]. Selenium deficit in animals shows afterbirth characteristics: white muscle disease with calves and a higher susceptibility to mastitis [GALLER, 2008].

The effects of the selenium supplementation of different kinds of meat are shown in Table 5 which was made in 2003/04.

Kind of meat	Muscle meat		Liver		Kidney	
	µg se/ kg of wet weight					
Veal	25	4-64	/			
Beef	18	8–26	258	205–291	1072	813-1487
Red deer	45	17–83	/			
Sheep/ lamb	/		429	184-445		
Horse	62	49–93	/			
Pork	84	66–106	538	351-689	1682	1494-1750

Table 5: Selenium supplementation in meat [SAGER, 2006]

The amount the plant is able to absorb depends on the kind of fertilization. Cereals especially absorb selenium and build it in the form of selenomethionine ($CH_3SeCH_2CH_2CH(NH_2)COOH$) into the protein fraction [UNTERWEGER, 2001]. In 1970, Finland supplemented fertilizers, which proved to be successful in increasing the Se intake of people. Inorganic selenium even reduced the need of supplementation of animal feeds [STOJANOVIC, 2000] but selenium fertilizers did not prevail. Edelbauer and Grausgruber (2003) found that with about two grams of sodium-selenate the Se content of grassland growth of accordant poor places can be increased. So, ruminant animals may get their adequate selenium supply. Toxification is impossible with this amount, but only under condition of exact apportionment of the fertilized place [EDELBAUER and GRAUSGRUBER, 2003]. In 2006, Sager and Hösch tested the uptake of selenium from a selenate containing NPK fertilizer. They found that there was a significant increase of the cereals' Se concentrations [SAGER and HOESCH, 2006].

Although the total selenium levels in soils, cereals, and grass samples are rather low, selenium fertilization is not done presently in Austria. There is no selenium fertilizer accredited [GERZABEK, 2010]. Although experiments by Sager and Hoesch (2006) showed that selenium contents can be elevated by soil supplementation, it is a controversial issue how the amounts really affect a person's health because toxicity is obvious [STOJANOVIC, 2000]. Manure has more selenium than agricultural soils, except from "bio"-farming [SAGER, 2006].

2.4.2. Selenium absorption by foods

In Northern Europe, primary Se sources in daily human nutrition are animal products. Selenomethionine, as well as the inorganic forms selenite and selenate, are the most frequently appearing forms of selenium in foodstuffs [UNTERWEGER, 2001].

Whether selenium is a nutrient or a toxicant depends on its concentration and on its chemical form. Selenium speciation is strongly affected by the oxidation state and pH of soil or water environment and it is dramatically affected by transformations mediated by living organisms, especially plants and microbes [CAI, 2003]. The daily selenium intake differs in countries, as shown in Table 6.

Country [Reference]	Remark	Selenium content (µg/day)
Austria [WILPLINGER and PFANNHAUSER, 1999]*		47.9*/ 48**
Belgium [ROBBERECHT et al., 1994]*		28.4-61.1*
Croatia [KLAPEC et al., 1998]*	women men	24.8* 32.2*
Finland**		30 -> 113**
France [LAMAND et al., 1994]*	women men	35* 43*
Great Britain [after VAN DOKKUM, 1998]*	TDS	63*
Greece**		95 // 110**
Netherlands**		67**
Slovakia [KADRABOVA et al., 1998]*	women men	32.6±6.6* 43.3±6.5*
Sweden [BECKER and KUMPULANIEN, 1987]*		44*/ 38**
Switzerland**		70**

Table 6: Daily selenium intake in different countries [*STOJANOVIC, 2000 and **SAGER, 2005; SAGER, 2006; modified]

The daily selenium supply depends considerably on gender. Men absorb about 25-30% more selenium with nutrition than women per day [OSTER, 1992]. The percentaged spreading of the daily absorbed selenium amount by German foods is presented in Figure 8.

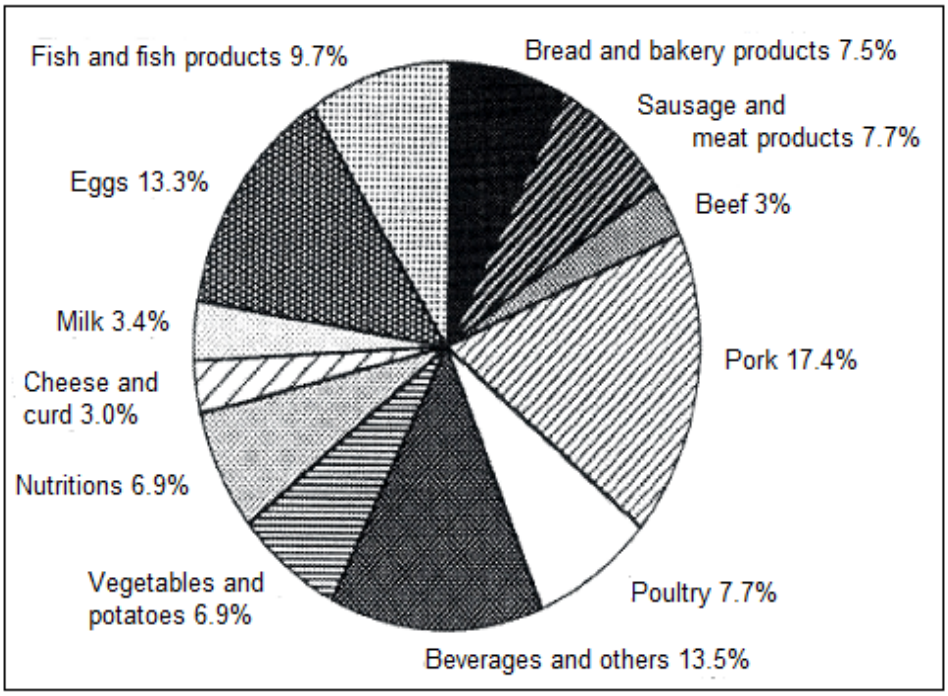


Figure 8: Spreading of daily absorbed selenium [OSTER, 1992; modified]

According to the *Bundesinstitut für Risikobewertung* (2004) the bioavailability of selenium in mixed nutrition is about 60-80%. The Se concentration depends on the protein content in food and mainly occurs through animal proteins. That is why primary fish, meat, offal and nuts are the selenium richest foodstuffs [STOJANOVIC, 2000]. As demonstrated in Figure 9 Se largely gets absorbed via proteins.

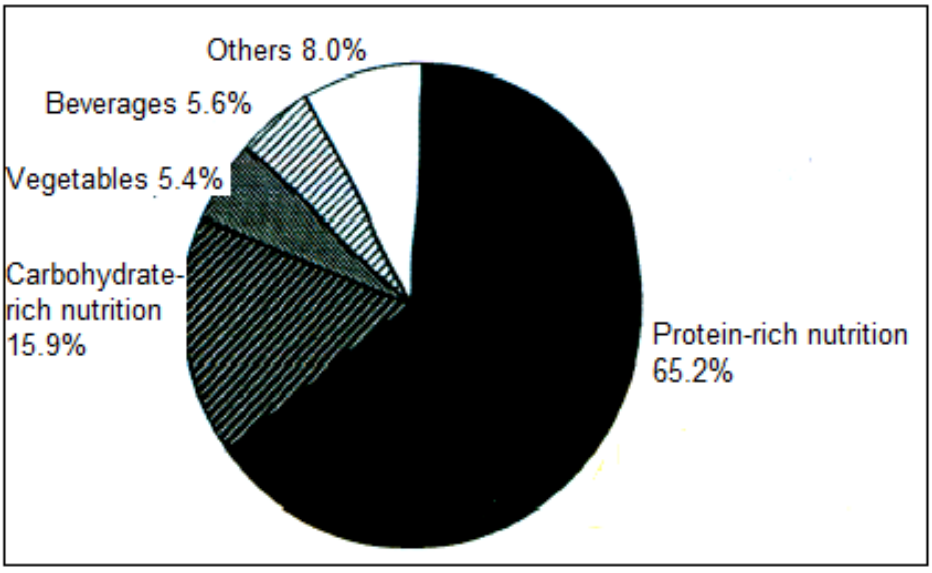


Figure 9: Spreading of daily Se intake on protein and carbohydrates [OSTER, 1992; modified]

The main amounts are absorbed from pork, which is - according to Sager (2005) – up to about 94% and poultry with about 21%, because of its meat and eggs. Pork as single food contributes to about 25% to the selenium supply, especially regarding sausages, which largely consist of pork [WISCHNEWSKI, 2005]. Indeed, the selenocysteine which is bound in meat gets absorbed well, but does not increase the Se level in blood and the GPx-activity [OSTER, 1992]. Generally, meat and fish appear to contribute about 40-50% of the total Se content [KIEFER and HABER, 2009].
Vegetables are selenium-poor foods, because they only meet the Se demands of 30% of women and of 23% of men [STÜCKLER et al., 2010]. L-selenomethionine constitutes 50 to over 80% of the total selenium in plants like cereals and soybeans which are grown on selenium-rich soils [AGUILAR et al., 2009]. The bioavailability of cereals is about 90-100% but cereals show, depending on their habitats, medial selenium contents [STOJANOVIC, 2000].

Commercially available fruit and vegetable juices may have higher Se contents than most potable and mineral waters. Furthermore, neither beer nor wine contribute to the Se supply, just like fats, oils, and sweets [SAGER, 2005 and SAGER, 2006].

2.4.2.1. Se content in animal and herbal foods

The two main selenium forms in food are selenomethionine or selenium yeasts and selenocysteine, which is to find in animal foodstuffs [STOJANOVIC, 2000]. Selenomethionine is contained in plant foodstuffs, like cereals, beans and mushrooms [REILLY, 1996]. The inorganic forms selenate (SeO_4^{2-}) and selenite (SeO_3^{2-}) only are to find in dietary supplements [STOJANOVIC, 2000].
For the human being, selenium from plants is better obtainable (80-100%) than from animal foods (15%) [SIMONOVA and PFANNHAUSER, 2008]. Selenium should ideally be absorbed in approximately same parts from herbal and animal foodstuffs [KIEFER and HABER, 2009].

The selenium content of foods exhibits great regional differences. The relative contributions of each food class to the total Se intake cannot be generalised because the Se contents depend on the derivation of the food [KIEFER and HABER, 2009]. The Se contents in foods of animal origin depend largely on the Se intake of the livestock. Most species have the proclivity to accumulate relatively great

concentrations of selenium in livers and kidneys. Therefore, these foods tend to be the selenium-richest sources [STOJANOVIC, 2000]. Nuts and seeds like sesame particularly are important Se sources for vegetarians. Selenium is also found in pistachios, paranuts, calves' kidneys, boletus, and soybeans [KIEFER and HABER, 2009].

Accumulation, low excretion, and low sensitivity to Se may explain higher Se levels in seafood than foodstuff of terrestrial origin. As fish muscle may contain about the double Se of meat, Se levels in fish have been found inverse proportional to the fat content [SAGER, 2006]. The biggest amount of selenium can be found in fishes and clams in the form of selenocysteine bound in proteins, but also selenate and selenium-containing lipo-proteins [SAGER, 2005]. Generally, the selenium content of freshwaterfish is considerably lower than that of seafish [OSTER, 1992]. Fish ingest most of their Se via nutrition, and not via water phase. Hemoglobin and glutathione peroxidase are higher in fish erythrocytes than in all other vertebrates [SAGER, 2006]. Both, lean fish (codfish, plaice or coalfish) and fatty fish (herring, mackerel, salmon, or tuna) are good selenium sources because of the composition of fatty acids [WISCHNEWSKI, 2005].

The iodine and selenium content of milk is not influenced by the fat content or the processing method (UHT, pasteurized). 400ml milk meets the demand to 28% of the daily supply of selenium. There are about 35µg selenium in one liter of Austrian milk [DGE et al., 2000]. The Se content of cow's milk generally reflects the selenium content of the soil, which shows a negative correlation [OSTER, 1992].

Herbal foods account only little for the selenium supply [HAMM, 2006]. Bread and bakery products, for instance, contain less selenium than meat products. Bread with a high wheat flour amount contains a little more selenium than bread with higher rye flour content. Whole-grain bread also contains considerably more selenium [OSTER, 1992]. Expressed on a fresh weight basis, vegetables and fruits provide only less than 8% of the total intake of the usual diet [STOJANOVIC, 2000].

Accumulation plants like *Astragalus bisulcatus* and broccoli strongly accumulate selenate from the soil [SAGER, 2006], while vegetable species like tomatoes or carrots show selenium concentrations of maximum 6µg/g [SIMONOVA and PFANNHAUSER, 2008]. Vegetables rich in starch and sugar are generally poor in

se. Some higher plants and fungi are known for a very strong enrichment of selenium (up to 300mg/kg), e.g. garlic or boletus (boletus edulis). Thereby, organoseleno compounds are built, which cannot be built in proteins, and so toxic effects are avoided [SAGER, 2005]. Moreover, mustard, caraway, cabbage, and broccoli also supply Se to the food chain. Vegetables grown on sewage-treated garden soil can contain twice as much selenium as vegetables from an untreated plot [REILLY, 1996]. The different Se contents of the food groups are demonstrated in Table 7. They should be seen as recommended values.

Animal foods (µg/100g)		**Herbal foods I (µg/100g)**		**Herbal foods II (µg/100g)**	
Beef	35	Cereals		Cabbage	18
Calf-kidney	260	Cereals	10*	Cucumber	to 60**
Cheese	to 11**	Corn, barley	to 2000**	**Pulses**	
Cow milk	5-9**	Wheat germ	110	Lenses	11
Egg yolk	30*/**	**Corn flour**	40**	Soy beans	60
Egg white	4-10**	Rice, polished	40**	White bean	22**
Fish, general	**13 – 140**/** 50*	Wheat-whole-grain-bread	55**	**Fruits**	
Herring	140	Whole grain bread	2*	Orange	3.5
Offal	40-550**/ 60*	Wheat bread	55	Banana	4.4
Meat (beef,veal, pork)	20-35**/ 20*	**Vegetables**		Grapes	2.8
Milk	9	Vegetables, general	1*	**Nuts**	
Milk products	4*	Potato	4-20**	Pistachio	450
Plaice	65	Mushrooms	100**	Brazil nut	100
Shrimps	41	Endive	13	**Alcohol**	
		Boletus	100**	Beer	to 19**
		Cauliflower	18		

Table 7: Selenium content of foods [KIEFER and KUNZE, 2008 and *RIEGER, 2009 and **ELMADFA and LEITZMAN, 1998; modified]

Determinations of Se concentrations in foods cannot exactly be apportioned on Austrian foods in general. Thus, some experts specify them in ranges as shown in Table 8.

Foods	Selenium content (µg/kg)
Animal foods	
- Beef	20-80
- Poultry	30-100
- Pork	50-150
- Liver	50-200
- Kidney	500-2000
- Fish and shellfishes	200-500
- Chicken egg	100-200
- Milk	5-20
- Cheese	20-200
Vegetable foods	
- Oils	<5
- Vegetables (potatoes, beans, celery)	10-30
- Edible mushrooms	20-100
- Fruits (apple, banana, orange)	<10
- Cereals	10-500
- Nuts (peanuts, walnuts)	20-200
- Paranuts (Brazil nuts)	2000-5000

Table 8: Selenium ranges of foods [Selen in der Umweltmedizin, 2006; modified]

2.4.2.2. Effects of processing on selenium levels in foods

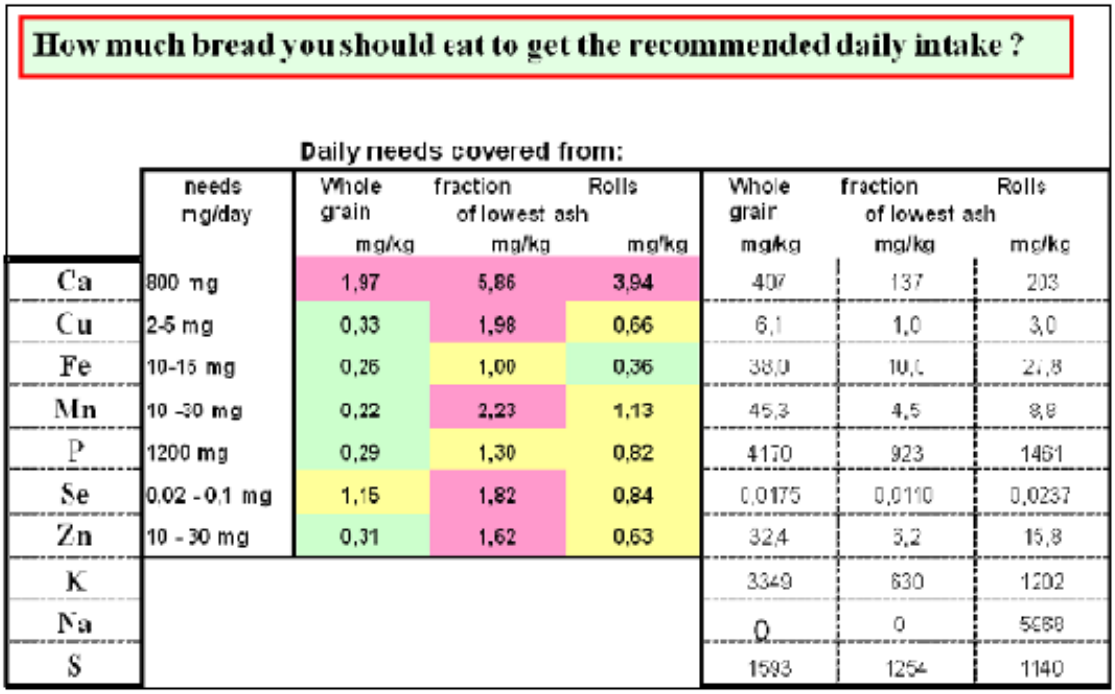
The selenium contents of foods are influenced by a number of factors. These are the types of foods themselves, the particular variety, climatic conditions during growing seasons, and the amount of biologically available selenium in the particular nutrient environment. The method of preparation and processing also influences the Se content of foods [STOJANOVIC, 2000].

In the course of time a lot of studies about the Se loss by food preparing were made. In 1972, Higgs at al. demonstrated that most cooking techniques like baking and boiling do not cause appreciable selenium losses from most foods. Furthermore, they found that dry heating of cereals caused a loss of 7-23% of the element, while boiling of asparagus and mushrooms resulted in a 29-44% loss. The conclusion of a more recent study about different types of cooking procedures (frying, grilling, boiling, and canning) of Greek foods was that "*the loss of selenium due to ordinary cooking is apt to be negligible*". Canning had the smallest effect, whereas frying and grilling caused the greatest Se loss. Losses do not always appear to occur and, if they do, the lost

amount appears to depend on the type of food and on the form of processing involved. Depending on the method of cooking employed, fish lost 36-46%, cereals 20-30%, vegetables 12-37% and peas, beans and cereal products 5-10%. American researchers found that there was an apparent increase in selenium levels in fish after having been cooked in various ways or canned. Cooking methods employed were baking, broiling and microwaving. The apparent increase was ascribed to loss of moisture during cooking. This finding is in agreement with those of Levander's group and appears to confirm the statement of the WHO Working Party's view that "usual cooking procedures cause little decrease in the Se content of most foods" [REILLY, 1996]. According to the most recent study by Stückler et al. (2008), processing has an important influence on the foods' Se contents [STÜCKLER et al., 2008].

Generally, heat has a negative effect on the selenium content in cereals, vegetables, fish and meat, depending on the duration and intensity [ELMADFA and LEITZMANN, 1998]. Se losses during grilling of pork obtained at various temperatures were similar, because higher temperatures led to shorter grilling times for the piece of meat to be ready. This effect is related to the instability and volatility of many selenium compounds. For seafood, however, most common cooking techniques, like baking or broiling, did not result in major Se losses. In the baking process, some Se may be lost, because the Maillard reaction of selonomethionine and glucose yields volatile seleniferous compounds. Smoking and cooking may convert selenide and selenite to selenate [SAGER, 2006]. Already the initial preparation of raw food can have an effect on the selenium level, e.g. milling can reduce the selenium amount in the final product. While the typical kinds of preparation of animal foods like roasting or frying show low selenium losses (about 15%), the cooking of herbal foodstuffs shows losses of about the half of the basal selenium content [STÜCKLER et al., 2008]. The processing of cereal grains and oil seeds can produce food products with selenium concentrations less than those of the parent materials due to the removal of relatively se-rich components. Milling products based on germ, bran and shorts (e.g., corn mill germ, rice bran) tend to contain higher selenium levels than the parent whole grains, and products based primarily on endosperm (e.g. corn flour, polished rice) [STOJANOVIC, 2000]. The higher the manufacture degree of cereals, the higher the selenium content of flours [ELMADFA and LEITZMANN, 1998]. In milling and processing, grains and cereals lose about 10% of their Se content due to local

heating and volatilization. Results from wheat-grinding and bread-baking experiments showed no significant selenium losses in the baking process. The selenium content is lower in flour than in whole grain because of dilution. The baked product has higher Se values than the dough because there is no volatilization [SAGER, 2006].



How much bread you should eat to get the recommended daily intake ?

Daily needs covered from:

	needs mg/day	Whole grain mg/kg	fraction of lowest ash mg/kg	Rolls mg/kg	Whole grain mg/kg	fraction of lowest ash mg/kg	Rolls mg/kg
Ca	800 mg	1,97	5,86	3,94	407	137	203
Cu	2-5 mg	0,33	1,98	0,66	6,1	1,0	3,0
Fe	10-15 mg	0,26	1,00	0,36	38,0	10,0	27,8
Mn	10 -30 mg	0,22	2,23	1,13	45,3	4,5	8,8
P	1200 mg	0,29	1,30	0,82	4170	923	1461
Se	0,02 - 0,1 mg	1,15	1,82	0,84	0,0175	0,0110	0,0237
Zn	10 - 30 mg	0,31	1,62	0,63	324	3,2	15,8
K					3349	630	1202
Na					0	0	5988
S					1593	1254	1140

Figure 10: Amount of bread to meet selenium demand [SAGER, 2006]

Another, still more topical study was made in 2007 by Sager and Werteker, who determined the loss of selenium on the way from cereal to the finished pastry product. The sort *Capo,* the main sort of the Austrian quality-wheat-crop growing for a long time was tested and the results of the baking tests did not show any losses of mineral nutrients [SAGER and WERTEKER, 2007].

Eggs, for instance, retained 55% of their Se after three minutes of boiling, and 38% after having been fried for five minutes [SAGER, 2006].

2.4.2.3. Antagonists and synergists of selenium

Many factors can affect the uptake and utilization of selenium by the human body [THOMSON, 2004]. Generally, all elements with a higher chemical affinity to sulfur belong to selenium antagonistic elements. As of its role in the GPx, selenium is likely to interact with other nutrients that affect the antioxidant-(pro)-oxidant-balance of the cell. It interacts, for instance, with trace elements and nutrients like the vitamins A, C, E and B_{12}, which get diminished [UNTERWEGER, 2001]. Thus, in combination with

vitamin E selenium has anti-inflammatory effects [HAMM, 2006] and diets low in vitamin E may increase the requirement for selenium [THOMSON, 2004]. Even vitamin C has an antagonistic effect relating to selenite [UNTERWEGER, 2001]. The GPx protects the lipid membrane from oxidative damage with lipid peroxidation [ELMADFA and LEITZMANN, 1998], which is inhibited by phospholipid-hydroxyperoxide-GPx (GPx_4) only if sufficient vitamin E is present in the membranes [ROVERI et al, 1994]. Very high doses of vitamin C can block the Se absorption [WISCHNEWSKI, 2005]. Protein-rich nutrition augments the availability of Se too [SAGER, 2006]. Biological effects of vitamin B_{12} get also diminished [SIMONOVA and PFANNHAUSER, 2008]. Pyrodoxin (vitamin B_6) is also a synergist because it is important in the application of selenium from selenomethionine [UNTERWEGER, 2001]. Further bringing forward factors for the intestinal bioavailability are antioxidants, like vitamin E and vitamin A (β-carotene) [WISCHNEWSKI, 2005]. A combination of antioxidants is more effective than very high doses of single antioxidants [ELMADFA and LEITZMANN, 1998]. So, in people with low selenium intakes, ascorbic acid can increase the availability of natural selenium in foods [REILLY, 1996]. Table 9 shows all the factors that affect the bioavailability of dietary selenium.

High available chemical forms of se:	**Poorly available chemical forms of se:**
Selenate, selenoamino acid	Reduced forms of se
Highly available food sources of se:	**Poorly available sources of se:**
High-se-yeast, wheat, alfalfa	Soybean, most meat and fish
Availability enhancers:	**Availability decreases:**
Restricted food intake, methionine proteins, vitamin E, ascorbic acid	Heavy metals (Pb, Hg, Cd, As), pyridoxine (vitamin B_6 deficiency), vitamin E and methionine deficiency

Table 9: Bioavailability of dietary selenium affecting factors [STOJANOVIC, 2000]

Selenium has strong interactions with heavy metals such as cadmium (Cd), silver (Ag) and mercury (Hg) that mainly appear in marine foods [THOMSON, 2004]. Cadmium influences the functions of essential elements like selenium but also zinc, iron, manganese, copper, calcium [ELMADFA and LEITZMANN, 1998]. Zinc influences the spreading of selenium in the organs [OSTER, 1992]. Mercury almost completely occurs in organic (methylated) forms in fish livers. Selenium also interacts with lead (Pb), thallium (Tl), arsenic (As), nickel (Ni), cobalt (Co) and bismuth (Bi) [SAGER, 2006 and SIMONOVA and PFANNHAUSER, 2008]. On the one hand, selenium protects against toxic effects of these metals but on the other hand, the binding of selenium on metals reduces its bioavailability [THOMSON, 2004 and REILLY, 1996].

2.4.3. Selenium in the human body

Selenium shows with about 20-30mg the fourth highest content of a trace element in the human body. It is only exceeded by iron, zinc and copper [MARKTL, 2001]. Higher concentrations can be found in offal, like liver and heart. The kidney is an organ that maintains a very considerable homeostatic control regarding the selenium content [OSTER, 1992]. The skeletal muscles exhibit the biggest store [ELMADFA and LEITZMANN, 1998], which contain about 47% of the total selenium existence of the organism [OSTER, 1992]. Further se-containing organs are the endocrine organs, mainly the gonadals, brain, thrombocytes [WISCHNEWSKI, 2005], erythrocytes and of course the thyroid [REILLY, 1996].

But in contrast to that, a more recent determination by Strehl (2006) demonstrates that under normal circumstances the human body contains 4-20mg selenium. In Table 10 the Se concentration in organs is demonstrated in an international comparison.

Country	Liver*	Kidney*	Skeletal muscle*	Heart*
Canada	0.390	0.840	0.370	/
USA	0.540	1.090	0.240	0.280
Japan	2.300	1.500	1.700	1.900
New Zealand	0.209	0.750	0.061	0.190
Germany	0.291	0.771	0.111	0.170
				*µg/g, wet weight

Table 10: Selenium concentrations in organs [OSTER et al., 1988; modified]

In the organism there is a depot in the form of protein-bound selenium that can be mobilized by deficiency. The protein-binding of selenium is also a kind of physiologic detoxification mechanism [OSTER, 1992].

2.4.3.1. Selenium metabolism

Bioavailability of selenium varies according to the source and the nutritional status [NAVARRO-ALARCON and CABRERA-VIQUE, 2008]. Generally, the bioavailability of organic-bound selenium of herbal (selenomethionine) and animal (selenocysteine) foods is much more effective than that of inorganic selenium [SIMONOVA and PFANNHAUSER, 2008]. The varied selenium compounds get metabolized in different ways regarding adsorption, organ spreading, and elimination [REILLY, 1996]. Selenium is more readily available in plants than in animal foodstuffs. Selenium absorption is 50% to more than 90% dependent on the concentration and on concomitant substances, independent from the selenium status [ELMADFA and LEITZMANN, 1998]. Nearly 50% of selenium in plasma is associated with albumin in people who consume a selenomethionine-rich diet [REILLY, 1996].

Various components of diet, including vitamins A, E and C, also affect selenium absorption in the gastrointestinal tract. Selenium metabolism is closely connected with protein metabolism [OSTER, 1992]. Selenium absorption appears in the duodenum, caecum, and colon [SIMONOVA and PFANNHAUSER, 2008].

Figure 11 presents the detailed Se transport and its absorption in the gastrointestinal tract.

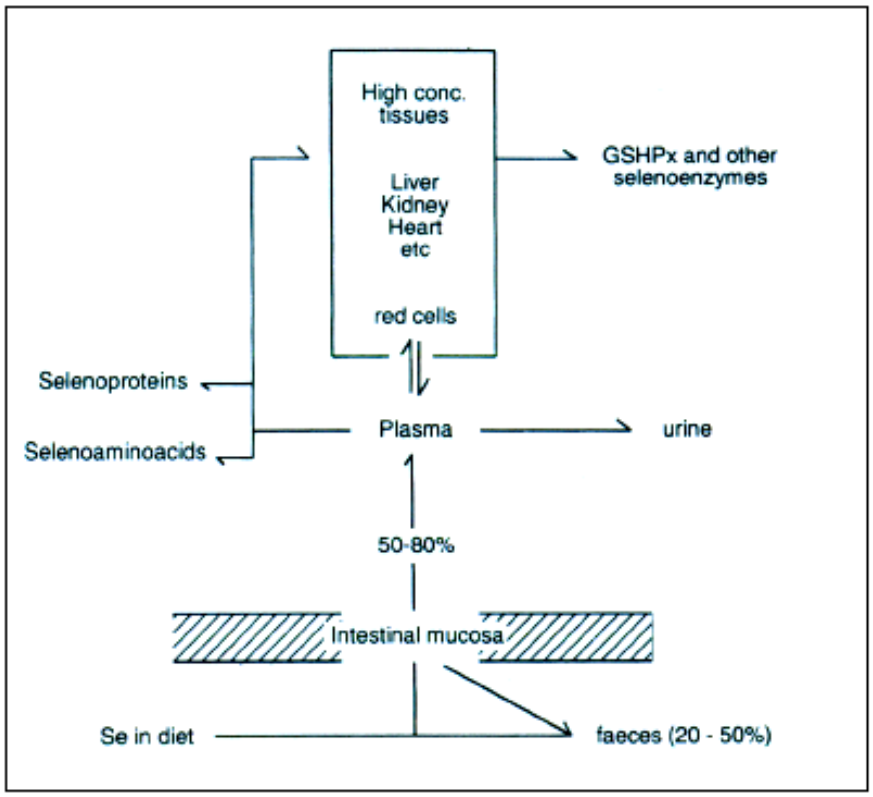


Figure 11: Selenium absorption [REILLY, 1996]

Selenite is absorbed by 60-80% and selenomethionine or selenate by more than 90%. Inorganic compounds get absorbed with drinking water and quickly get metabolized. Selenate changes into selenite and afterwards into dimethylselenide. In this form, selenides can be built into special seleno proteins [UNTERWEGER, 2001].

Bleys et al. (1993) found that elevated serum selenium is associated with increased serum concentrations of total cholesterol, LDL or HDL cholesterol. Thus, the selenium absorption is strongly coupled on cholesterol-rich foods [OSTER, 1992].

Dietary selenomethionine is metabolized by the body to other functional selenium forms, like selenocysteine, or there is methionine metabolism and it is stored as selenoprotein [AGUILAR et al., 2008], including hemoglobin and plasma albumin. In contrast to that, selenite and selenocysteine are directly used in the organism for the synthesis of GPx. Selenocysteine and -methionine are actively transported in humans by the same transport mechanism as used by its sulfur analogue [REILLY, 1996].

Absorbed selenium is transported into blood from the gut mainly bound to blood lipoproteins, especially to a very low-density-β-lipoprotein fraction (VLDL). The process uses reduced glutathione and involves the enzyme glutathione reductase. This requires an initial reduction within erythrocytes of selenium to selenide. Besides the red cells, it achieves its highest concentration in the liver, spleen, heart, nails, and tooth enamel. It is incorporated into a variety of selenoenzymes, including GPx, and non-specific selenoproteins [REILLY, 1996]. The relationship between selenium in food and selenium in tissue can be seen in Figure 12.

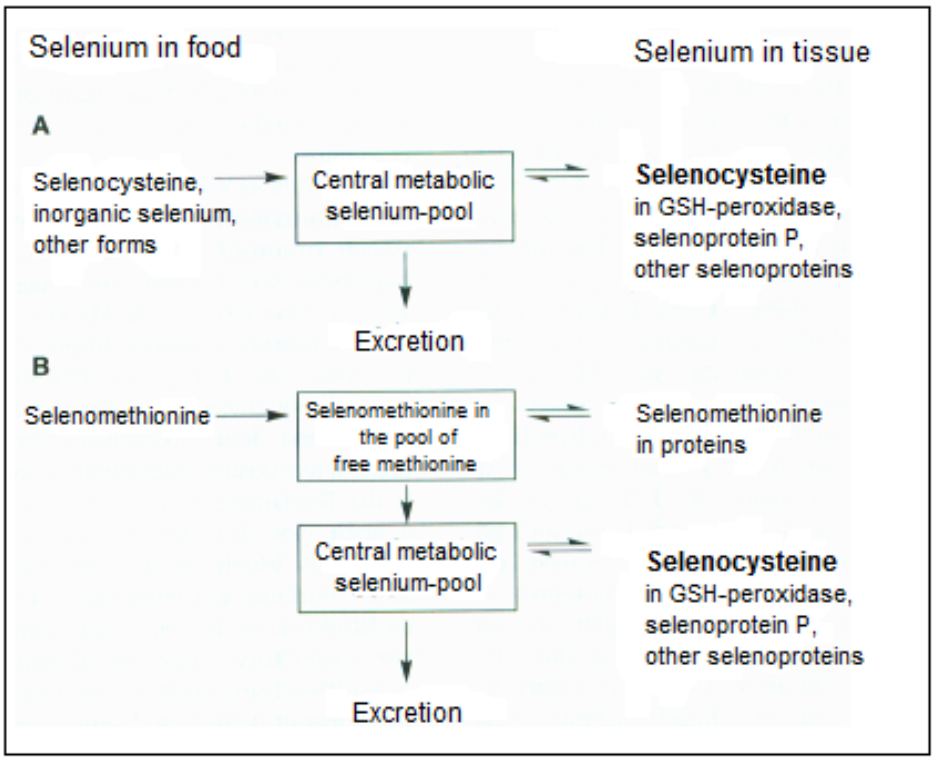


Figure 12: Selenium conversion from food to tissue [ELMADFA and LEITZMANN, 1998; modified]

Selenomethionine either changes to selenocysteine, or unspecifically gets enriched in proteins and so it is later used in protein and amino acid elimination for the synthesis of selenide [UNTERWEGER, 2001]. That is why selenomethionine as a metabolic inactive selenium pool is retained for a long time in the organism. That possesses an unregulated storage capacity for selenite or selenocysteine. On the contrary, organic bound selenium gets absorbed as selenomethionine just as methionine through an active transport mechanism, while the absorption of selenite in the brush border membrane mainly appears with passive diffusion. The selenate absorption appears with the help of a sodium-dependent carrier-mediated transport.

Selenomethionine seems to be more efficient to be absorbed a retained than inorganic selenium compounds. Selenite and selenocysteine end in a common metabolic way, which serves as selenide to a targeted integration in selenoproteins [ELMADFA and LEITZMANN, 1998]. Figure 13 presents the outline of pathways of the Se metabolism.

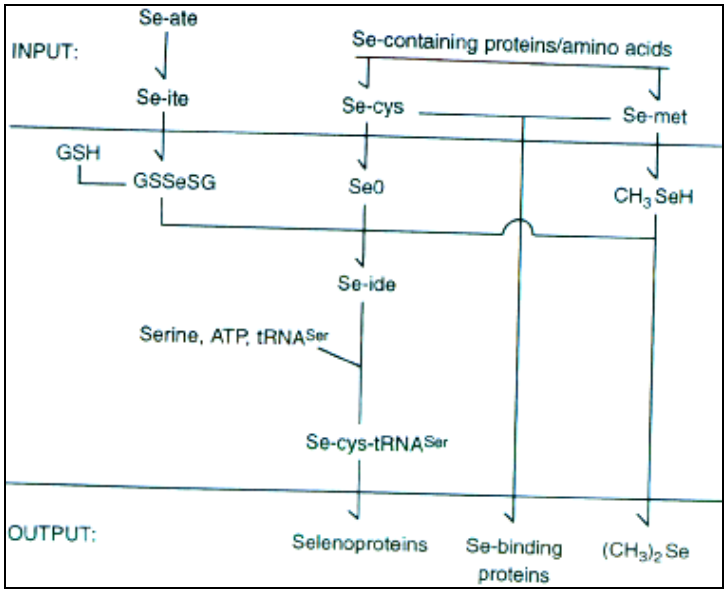


Figure 13: Pathways of selenium metabolism [REILLY, 1996]

The amounts and proportions of each type of excretion depend on the level and form of selenium in diet. Selenium is mainly eliminated by three distinct routes: in urine via the kidneys, in feces from the gastrointestinal tract and in the expired air via the lungs. The elimination takes place at about 60% of urine by which the homeostasis in blood gets regulated by the kidneys and at about 40% with feces. But also small amounts are eliminated through sweat and skin and through biliary and pancreatic secretions. Selenium is also lost by the body to a limited extent in hair, nails, and breast milk [REILLY, 1996]. Particularly, through mother's milk selenium elimination is about 5-18µg/l and there is no placenta barrier [ELMADFA and LEITZMANN, 1998]. Of course, by diarrhea there is a higher Se elimination, which can be above the supply. The selenium elimination by urine is calculated with 9-25µg and by feces with 8-23µg per day [OSTER, 1992]. Much of selenium excreted via the kidneys is in form of good soluble trimethylselenonium. The Se elimination of urine correlates positively with the concentration in serum, whole blood and hair. Fecal selenium consists largely of unabsorbed dietary selenium, as well as in biliary, pancreatic, and intestinal secretions [REILLY, 1996]. The muscle mass adds to the Se elimination too

and that is why about 50% of total body selenium supply is to be found in muscles. The Se requirement of a population also can be assessed when its elimination amount of the kidney and feces is measured [OSTER, 1992].

2.4.3.2. Selenium functions in the immune system

Selenium defends the organism from environmental damage and influences the function of all components of the immune system [ELMADFA and LEITZMANN, 1998]. Typical functions of phagocytes like chemotaxis, phagocytosis and fungicide or bacterial activities, depend on the selenium concentrations within the cells. The cytotoxic capacity of lymphocytes is affected by selenium too. Furthermore, the antibody synthesis and the tumor necrosis factor are positively affected by selenium [ELMADFA and LEITZMANN, 1998]. Besides se, also zinc is important for the production of immune cells and antibodies in the human body [HAMM, 2006]. Table 11 shows the most important functions of selenium.

Selenium's functions
- Acts antioxidative as cofactor of the glutathione peroxidase (GPx)
- Possesses enzyme-independent radical scavenger functions
- Develops in the cell specialization an anti-inflammatory effect
- Is antagonist of heavy metals, like mercury and cadmium
- Modulates the immune system
- Has anticancerogenic effects
- Has tasks in the thyroid metabolism as cofactor of type-I-deiodinase
- Has further but not yet determined functions as component of other selenoproteins

Table 11: Functions of selenium [SIMONOVA and PFANNHAUSER, 2008; modified]

In serum or plasma, selenium is bound to 40% on the GPx, to 10% on albumin, and to 50% on selenoprotein P. High blood selenium supplies the organs with sufficient Se to synthesize selenoenzymes [ANGSTWURM et al., 2007]. Selenium is capable of exerting multiple actions on endocrine systems by modifying the expression of at least 30 selenoproteins [BOOSALIS, 2008]. Selenoproteins are redox catalysts and have selenocysteine at their active sites. If this is replaced by its sulfur analogue cysteine, the activity of the enzyme is markedly reduced [REILLY, 1996]. Selenoproteins function as a defensive mechanism for oxidative stress, for the regulation of thyroid hormone activity, and for the redox status of vitamin C and other

molecules [BOOSALIS, 2008]. Selenoenzymes defend thyroid cells from oxygen-radicals, which are constantly built in the thyroid and can also have a share in the deletion of thyroid cells. Thus, they are able to curb chronic inflammation processes. Furthermore, selenoenzymes can modulate immune reaction and can lower inflammatory reactions [MERCK, 2009]. The concentrations of selenoenzymes are not augmented by higher selenium intake [SIMONOVA and PFANNHAUSER, 2008].

In eucaryontic organisms four different families of selenoproteins are specified. These are the glutathione peroxidases (GPxs), the thioredoxin reductases (TRs), the iodothyronine deiodinases (Ds; iodothyronine 5'-deiodinases)) [BECKETT and ARTHUR, 2005 and KIEFER and HABER, 2009] and the seleno-phosphat-synthetases. Table 12 presents the specific selenoproteins of mammals.

Selenoproteins	Occurrence	Function
Gluthatione peroxidase:		
-Cytosolic or rather classic GPx (cGPx) -Gastrointestinal GPx (GI-GPx) -Plasma-GPx (pGPx) -Phospholipid-Hydroperoxide GPx (PHGPx) -Spermal GPx (snGPx)	-In cell cytosol of almost all tissue types -In cells of the gastrointestinal tract -In extracellular fluids, predominantly in the kidneys -In the cytosol or membrane-associated in different tissues, mitochondria of spermatozoa -In the nucleus of spermatids, spermatozoa, testicle	-Catalyses the reduction of hydrogen peroxide and different other soluble organic peroxides (generally) -Participation in the antioxidative defense system against free radicals and relative molecules -Support of vitamin E, which catches free radicals (generally); defense system against orally absorbed lipid-hydroperoxides (GI-GPx) -Protection of biological membranes against oxidative damage; participation in inflammatory and apoptosis-processes; participation in the spermatogenesis (PHGPx) -Influence on sperm maturation and fertility through Disulphide-Cross-Linking/Reorganisation of DNA (snGPx)
Iodothyronine deiodinases:		
-Type-1-deiodinase -Type-2-deiodinase -Type-3-deiodinase	-Thyroid, liver, kidney, central nervous system -Brain, placenta, pituitary, brown adipose tissue, central nervous system, skeletal muscle, myocardium -cental nervous system, skin, placenta	Catalysis of activation and inactivation of thyroid hormones, development of the fetal brain
Thioredoxin reductases:		
-Thioredoxin reductase 1 -Thioredoxin reductase 2 -Thioredoxin reductase 3	(in different tissues)	Catalysis of NADPH-dependent reduction of oxidised thioredoxin; Exertion of influence on DANN-synthesis or rather on regulation of transcription factors, cell growth, apoptosis inhibition
Selenophosphate-synthetases:		
Selenophosphate-synthetase 2	(in different tissues)	Catalysis of the reaction of selenide with AMP; product selenophosphate is selenium-donor by the biosynthesis of selenocysteine

Table 12: Specific selenoproteins [SIMONOVA and PFANNHAUSER, 2008; modified]

The GPx and thioredoxin reductases are important compounds responsible for the maintenance of the redox system in all cells including the immune competent cells. The activity of these enzymes is mainly regulated by the availability of Se [ANGSTWURM et al., 2007]. The best known and most important biochemical function of selenium is the integral component of the glutathione peroxidase (GPx) which catalyzes the reduction of organic and inorganic hydroperoxides. In erythrocytes, selenium protects hemoglobin against oxidative damage that is caused by hydrogen peroxide (H_2O_2) [ELMADFA and LEITZMANN, 1998]. The prevention of lipid peroxidation in cell membranes and organelles is very important, as the build-up of cell-toxic compounds can be avoided in this way. This reaction happens through a radical-stop-mechanism. Generally, the brain, the reproduction organs and the endocrine organ system show a preferred selenium supply, while blood plasma, erythrocytes, heart, liver and skeletal muscles in this hierarchy are in a lower range. That is why deficit symptoms with selenium undersupply become manifest in these organs first [SIMONOVA and PFANNHAUSER, 2008].

Four selenium-dependent GPx with different specificities to hydroperoxides and localisation (cytosol, plasma and phospholipides) are known [ELMADFA and LEITZMANN, 1998 and STOJANOVIC, 2000]. These are the cellular-, the gastrointestinal-, the extracellular- or plasma-, and the phospholipid hydroperoxide-glutathione peroxidase [SAGER, 2006, p.122]. The GPx-3 activity is the main GPx activity in serum and is negatively correlated with the severity of the diseases [ANGSTWURM et al., 2007].

Three types (type 1-3) of an iodothyronine-5'-deiodase are known as selenium-dependent enzymes which are involved in thyroid metabolism [STÜCKLER et al., 2010]. Type I-iodothyronine-5'-deiodase catalyzes the conversion from thyroxin (T_4) to the biologic active form 3, 3', 5'-triiodothyronine (T_3). Thus, selenium deficiency may be partially implicated in some types of hypothyroidism [ELMADFA and LEITZMANN, 1998 and STOJANOVIC, 2000]. Generally, selenium deficiency is likely to impair immunity [HATFIELD, 2001] and leads to immune suppression. Selenium deficiency leads to reduced phagocytose activity and augments the susceptibility to infections. The most interesting fact is that it is connected with the appearance of thyroid diseases [ELMADFA and LEITZMANN, 1998]. The reduction of specific selenoproteins as a result of selenium deficiency contributes to the symptom causes

associated with the diseases, which are a plausible mechanism of too low selenium intake [HATFIELD, 2001].

In areas with severe selenium deficiency there is a higher incidence of thyroiditis due to a decreased activity of selenium dependent GPx activity within the thyroid cells. Even mild selenium deficiency may contribute to the development and maintainance of autoimmune thyroid diseases. So, severe nutritional selenium deficiency lowers the general immune competence and leads to an increased rate of thyroid cell necrosis and to an invasion of macrophages [GÄRTNER et al., 2002]. The neutralization of oxygen radicals is also reduced by selenium deficiency, because the contra regulated selenium-dependent antioxidative protection systems (GPx) are only active in a limited way [STOJANOVIC, 2000 and HEUFELDER, 2006]. The phagocytose activity is limited too, so an augmented sensitivity against bacterial infections occurs [ELMADFA and LEITZMANN, 1998]. Donations of low selenium doses lead to an amplification or the recreation of the immune function [SIMONOVA and PFANNHAUSER, 2008].

2.4.3.3. Recommendations for an adequate selenium supply

An adequate selenium intake is very important because selenium deficiency diseases but also excesses resulting in toxicity are reported frequently [CAI, 2003 and SAGER, 2006]. But reference areas only are based on the estimations of studies [THOMES, 2004].

The World Health Organisation (WHO) has to set recommendations that must apply to many different countries around the globe. Additionally, the basal requirement of selenium should be defined referring to the "*intake needed to prevent pathologically relevant and clinically detectable signs of impaired function attributable to inadequacy of the nutrient*". This suggestion was taken from the quantity needed to protect against Keshan disease. The WHO also targeted the values on the GPx activity saturation in blood plasma of $^{2}/_{3}$ of the maximum and advises 30µg for women and 40µg se/day for men [WHO, 1996]. The mean intakes of dietary Se shows Table 13.

Life Stage	Age (yrs)	Selenium Basal Intakes (µg/day)	Se Normative Intakes (µg/day)
Infants	0 – 1.0	3 – 6	6 – 12
Children	1 – 10	10 – 14	20 – 25
Males 10–18 18+		 16 – 21 21	 30 – 40 40
Females 10 – 18 18+		 16 16	 30 30
Pregnancy		18	39
Lactation 0-3 months 3-6 months 6-12 months		21 25 26	42 46 52

Table 13: Mean intakes of dietary selenium [HATFIELD, 2001; modified]

The German, Austrian, and Swiss Nutrition Societies established an adequate daily dietary selenium intake for adults in the range between 30 and 70µg [D-A-CH-Reference values, 2000]. In Europe, an adequate supply for an adult is reached in the area of 20-100µg selenium/day but a saturation of GPx activity is not reached by the usual selenium supply [ELMADFA and LEITZMANN, 1998 and STREHL, 2006]. According to Aguilar et al. (2008), the daily nutrition-caused selenium supply in the European population lies between 27-70µg and the more recent determination of the following year by Aguilar et al. (2009) showed a Se level of 24-89µg.

The current recommended dietary intake of selenium in humans is between 55 and 75µg per day. It is also based on the selenium intake that induces the maximum activity of the GPx in plasma and erythrocytes [SAKR et al., 2007 and BECKETT and ARTHUR, 2005]. The estimated values of an adequate selenium intake [DGE, 2008] are shown in Table 14.

Age	Selenium (µg/ day)
Infants	
0 to < 4 months	5–15
4 to < 12 months	7–30
Children	
1 to < 4 years	10–40
4 to < 7 years	15–45
7 to < 10 years	20–50
10 to < 13 years	25–60
13 to < 15 years	25–60
Adolescents and adults	
15 to < 19 years	30–70
19 to < 25 years	30–70
25 to < 51 years	30–70
51 to < 65 years	30–70
65 years and >	30–70
Pregnants	30–70
Lactating	30–70

Table 14: Reference values of selenium intake [D-A-CH-Reference values, 2000]

The recommended values of DACH are 50µg (30-70µg) of selenium [DGE et al., 2000]. For prevention of thyroid dysfunctions all women with child's wish in case that they have a healthy thyroid, should daily take 75µg selenium [BOHNET, 2009].

The minimum daily selenium amount for the human being is between 16-70µg. Relating to the body weight it is between 0.3-1.1µg/kg [OSTER, 1992]. The Tolerable Upper Intake Level (UL) is about 400µg/day [DGE et al., 2008 and FOOD and NUTRITION BOARD, 2000]. In contrast to that, the *Scientific Committee on Food* (SCF) arrived at an UL of 300µg/day [AGUILAR et al., 2009]. The SCF calculated a daily selenium supply of 40µg, which results from a population reference supply of 55µg/d of men and women [ELMADFA and LEITZMANN, 1998 and STREHL, 2006].

According to the SCF, the selenium supply of about 850µg/day could be fixed as No-Observed-Adverse-Level (NOAEL) value for clinical selenosis [AGUILAR et al., 2009]. An acute selenosis can be expected by adult people (70kg) from a unique oral ingestion amount of more than 3500µg selenium, which equates to a dose of 50µg selenium per kg of body weight [SIMONOVA and PFANNHAUSER, 2008]. But even toxicity values vary [STREHL, 2006].

In the Recommended Dietary Allowance (RDA), published approximately every ten years during the period 1980 to 2000, selenium has gained more and more attention as a factor of great importance in human nutrition in the last years. The were proposed on the basis of extrapolation from animal experiments. The upper limit of selenium intake for adults was based on that maximal intake [HATFIELD, 2001].

Mean value of the *Estimated Safe and Adequate Daily Dietary Intakes* (ESADDI) for adults is about 125µg/day, followed by the RDA of 70µg/day for adult males and then the 2000 RDA of 55µg/day for adults of either sex. The RDA during lactation provided sufficient selenium to avoid depletion in the mother and permit satisfactory selenium content in breast milk [HATFIELD, 2001]. Table 15 shows the ESADDI and the RDA of different life stages.

Life stage	**Age (years)**	**ESADDI (1980)**	**RDA (1989)**
Infants	0–0.5 0.5-1	10–40 20–60	10 15
Children	1–3 4–8 7–10 11+	20–80 30–120 50–200 50–200	20 20 30 /
Adults (generally)		50-200	
Males	11–14 15–18 19–24 25–50 51+		40 50 70 70 70
Females	11–14 15–18 19–24 25–50 51+		45 50 55 55 55
Pregnant women			65
Lactating women			75

Table 15: ESADDI and RDA for selenium (µg/day) [HATFIELD, 2001]

With the EAR - which is 45µg selenium/day - a difference in the prevalence of an insufficient supply can be found. The various reference values include special percentages of secureness. The RDA is set by supposing a variation coefficient (CV) of 10% because information is not available on the standard deviation of the selenium requirement. "*The RDA is defined as equal to the EAR plus twice the CV to cover the needs of 97-98% of the individuals in the group (therefore, for selenium the RDA is 120% of the EAR). The calculated RDA is rounded to the nearest 5 µg*". The

RDA for both men and women is 55µg/day. The UL for adulescents is 400µg/day, which is based on the adverse effects of selenosis [DRI, 2000].

Generally, it is advised to absorb about 1µg selenium/kg of body weight daily [OSTER, 1992].

2.4.3.4. Selenium deficit and risk groups

Selenium deficit is associated with a lot of serious diseases like severe cardiovascular diseases but also diseases of joint and musculoskeletal system [STÜCKLER et al., 2008 and KÖHRLE and GÄRTNER, 2009]. Further possible consequences of selenium deficiency are arteriosclerosis, miscarriage, neurological disorders, depression, and augmented cancer risk [HATFIELD, 2001].
Selenium deficit occurs because of selenium-poor nutrition, special diets, and liver cirrhosis [LOHMANN, 2008]. Deficit symptoms appear from a selenium supply of about less than 20µg/d [SIMONOVA and PFANNHAUSER, 2008].

Two diseases are very often mentioned in the context of selenium deficit, namely Keshan and Kashin-Beck disease [STOJANOVIC, 2000]. Keshan disease first occurred in 1935 in selenium poor areas of the iodine deficient areas of China, particularly in Keshan country. It is an endemic cardiomyopathy that afflicts the peasant population. The average Se intake of Keshan patients has been estimated with about 10µg/day, approximately half of what was found in low selenium areas [HATFIELD, 2001]. The second well known Se deficit disease is the Kashin-Beck disease, which is basically an osteoarthropathy. It is endemic in a selenium and iodine deficient area of China. There, residents also consume diets largely consisting of homegrown grains. Like Keshan disease, this disease is limited to poor, isolated communities with very low concentrations of both iodine and selenium in the soil, agricultural products, and human tissues. Selenium concentrations in staple foods of Keshan-Beck endemic communities were reported to be about one-eighth of that found in areas outside the band of iodine and selenium deficiency. The selenium enrichment of table salt led to a drastic reduction of new cases. There is no genetic factor involved because immigrants also developed the same symptoms [SIMONOVA and PFANNHAUSER, 2008 and HATFIELD, 2001].

The registered risk groups of Se deficit are shown in Table 16. These may have nutritive causes or the elevated selenium elimination by the human body causes it.

A.	**Groups with the risk of an nutritive selenium deficit**
-	Strict vegetarians (vegans),
-	In cases of extremely unbalanced diet, e.g. alcoholics,
-	With tube-feed nourishment, e.g. PKU patients,
-	Parenteral nourished patients,
-	Dialysis patients,
-	In cases of starvation,
-	With Anorexia Nervosa,
-	With Bulimia.
B.	**Groups with the risk of a selenium deficit due to losses**
1.	**Losses through faeces**
-	With heavy long-lasting diarrheas,
-	With maldigestion,
-	With malabsorption (malabsorption syndrome),
-	With laxative abuses
2.	**Losses through urine**
-	With glomerular and tubular kidney damages with proteinuria,
-	With Nephrotic Syndrome,
-	With negative nitrogen balance,
-	With diabetes insipidus,
-	With diuretica therapy.
3.	**Through loss of blood**
-	With heavy hemorrhoidal bleedings,
-	Hypermenorrhoeas.
4.	**Losses during lactation**
-	In long-lasting lactation

Table 16**:** Risk groups of selenium deficit [OTTO and VON MÜHLENDAHL, 2008; modified]

In general, there are five risk groups of selenium undersupply. The first group includes prematurely born babies and children with hereditary metabolic diseases like phenylketonuria (PKU) and maple syrup urine disease. These children have comparatively low selenium stores because they are mainly fed with low selenium breast milk for the first twelve living weeks. Thus, they develop a significant selenium deficit. Babies who receive cow's milk nutrition, a suboptimal selenium supply can be eliminated by an adjustment of the selenium content [ELMADFA and LEITZMANN, 1998]. The second risk group are patients who receive either enteral nutrition (EN, tube feeding) or total parenteral nutrition (TPN, intravenous feeding) for extended periods of time. These commercial nutrient solutions do not contain adequate amounts of selenium. They often contain less than 5µg/dl. Selenium supplements

normalize the selenium contents of plasma [HATFIELD, 2001]. Among the third group there are alcoholics who have abased plasma selenium concentrations and reduced mean selenium elimination in urine. But an adequate selenium supply with nutrition can correct the selenium deficit without any supplementation. Low serum selenium concentrations can also be found with mild and heavy forms of alcohol-qualified liver diseases [ELMADFA and LEITZMANN, 1998]. Patients nourished with special diets like extreme vegetarians, patients with renal protein losses and gastro-intestinal complications like Crohn's disease belong the fourth risk group [OSTER, 1992]. A bigger deficit is observed in vegans. In contrast to them, lacto-vegetarians and lacto-ovo-vegetarians have a lower risk of Se deficit. Gmnivores tend to absorb higher Se amounts than vegetarians [SAGER, 2006]. Finally, pregnant women, breastfeeding mothers but also young women with hypermenorrheas are among the last risk group [OSTER, 1992]. Pregnant women should be examined carefully relating to their Se status. Yet, a study by Golubkina and Alfthan (2002) indicated no great selenium deficiency in pregnant women, although serum selenium concentration decreased during the progression of pregnancy. The serum cord blood selenium levels correlated with the mother's selenium status and a suboptimal selenium intake by expectant women predisposed their infants to a low Se status [GOLUBKINA and ALFTHAN, 2002]. Thus, pregnant women should pay special attention to an adequate Se intake [OSTER, 1992]. Contrary to cows, higher Se plasma levels in women do not necessarily lead to higher levels in human breast milk, which is concluded from Japanese data [SAGER, 2006]. Lactating mothers also act as puffer and so protect the child of too high Se amounts [AGUILAR et al., 2008].

Anyway - apart from the mentioned risk groups - there is no definitive selenium deficiency in middle Europe [ZIMMERMANN and KÖHRLE, 2002].

2.4.3.5. Determination of the selenium status

Generally, a biomarker is the only possible way to assess the adequacy of intake, and selenium is the best example for this. An ideal linear correlation between intake and blood level is very important, especially for nutrients which have wide concentration variations within individual foods [FREISLING, 2007]. Furthermore, it is the effective level of selenium in the body in relation to its functions contributing to the well being of the organism but it is not simply the total of its quantity in the body. The

tissue selenium content correlates with the serum selenium content [OSTER, 1992]. It is important to determine the selenium status when the relationship of diet to various selenium-related conditions is questionable but also when the effectiveness of dietary intervention and selenium supplementation is being considered [REILLY, 1996].

The selenium status in humans is primarily influenced by its intake [STOJANOVIC, 2000]. Its determination, however, is complicated because of the complex selenium metabolism [OLTERSDORF, 1995]. When there is an adequate selenium supply there is a very fast reaction of the blood status [FREISLING, 2007].

The selenium status of the population can be diagnosed with Se concentration in serum, plasma, whole blood and erythrocytes, relating to hemoglobin. The Se content in serum is used for calculation of the actual selenium status [SIMONOVA and PFANNHAUSER, 2008]. It generally consists of the selenium content of serum proteins, the Se content of the glutathione peroxidase in serum, and the Se content of a still unknown protein [OSTER, 1992]. The plasma selenium level is also an index of short-term status. It is used for the diagnosis of medium-term limited aberrances from the normal status. Although plasma selenium is not generally considered to be an ideal biomarker of the selenium status, it is the most widely used [UNTERWEGER, 2001].

On the contrary, total blood reflects the selenium long time status of a person better. The Se content of erythrocytes is composed of Se which is contained in GPx (maximum 16% of the erythrocytes) and the selenium content of hemoglobin (80-90%) [OSTER, 1992]. Erythrocyte-selenium also gives a long-term measure because of the long life span of these cells [REILLY, 1996]. Erythrocytes and thrombocytes namely store selenium in the form of GPx in long-ranging ways, at least over the whole life-time of blood cells. The activity of GPx of erythrocytes only stays in direct correlation with the blood selenium content in populations with relatively low selenium supply [ELMADFA and LEITZMANN, 1998]. As of the shorter life span of thrombocytes of 8-14 days, the blood plate GPx, in addition to the plasma selenium determination, is a sensible parameter for selenium depletion or repletion [SIMONOVA and PFANNHAUSER, 2008; SELEN in der UMWELTMEDIZIN, 2006 and WISCHNEWSKI, 2005]. In Europe, selenium status is not adequate for the

optimal GPx or immune function, as determined by selenium concentrations in serum, plasma or selenium intake [SAKR et al., 2007].

A review by Asthon et al. (2009) evaluated all possible kinds for the selenium determination in humans. It was found that plasma-, erythrocyte- and whole blood-selenium but also plasma selenoprotein P, and plasma, platelet, and whole-blood glutathione peroxidase activity all respond to the changes in selenium intake. On the contrary, urine, feces, and nails are not adequate indicators of the individual selenium status. When foods have high selenium contents, it gets augmented in urine and blood. Selenium contents in urine are only measured in exceptional cases like intoxication [ELMADFA and LEITZMANN, 1998]. Selenium evaluation in hair is not very clear, because even some hair shampoos contain selenium [OSTER, 1992]. Selenoprotein P accounts for 50% of selenium in the blood and was found to be a useful biomarker of the Se status, especially in populations with relatively low to moderate intakes [ASHTON et al., 2009] because it responds to different dietary selenium forms. A topical study about selenoprotein P was made by Hurst et al. (2010) whose results provide important evidence for deriving estimated average Se requirements in adults [HURST et al., 2010]. However, it still cannot be used routinely because there are existing methodical problems for standardization. The limited stability of the enzymes makes the determination difficult [WISCHNEWKI, 2005 and SIMONOVA and PFANNHAUSER, 2008].

Summing up, more information is needed for all potentially useful biomarkers to evaluate strengths and limitations in different population groups. These include the effects of varying intakes and the duration of intervention [UNTERWEGER, 2001].

III) EXPERIMENTAL PART

3.1. Subjects and study design

The study was made in the *Wilhelminenspital* and *Kaiserin Elisabeth Hospital* in Vienna in cooperation with Dr. Siroos Mirzaei. Data collection is based on the principle of the cross-selectional study and covers the period from October 2009 to January 2010. Patients were selected from the outpatients of the department of Nuclear Medicine in the both hospitals and were informed and asked to take part in the study. So, all have voluntarily entered the study.

Required data from a total of 216 subjects were collected by interviews and laboratory determinations. Although some subjects have foreign roots, all of them are living in Vienna, Austria. The study population demonstrates a randomly sample of the basic population largely with thyroid dysfunctions. Both, patients who came to the hospital for thyroid gland examinations for the first-time and patients who came for a check up were incorporated into the study. Specifically, only from 212 subjects could all data be obtained. From the other four people only their thyroid data and some blood Se levels could be got with their agreement but no interviews. Unquestionably, these data also were included into this research for suitable analyzes.

At the beginning of this study a Food Frequency Questionnaire (FFQ) and additionally, a second questionnaire about general nutrition and case history, were worked-out. The FFQ was developed for the exact calculation of the individual Se intake by special se-rich foods that can be purchased in Austrian supermarkets. The second questionnaire included socio-demographic data, eating habits, medical history, and thyroid values. Therefore, thyroid data from the last examination were taken from the patient's card indices (Laboratory I) and the actual thyroid blood data were made at the same day of the selenium sampling (Laboratory II). Thus, the interview about the subject's nutritional habits, the FFQ and the blood collection for selenium analysis and for the determination of thyroid values were handled within one day. Often it was possible to ask the participants in their waiting time, during two examinations so as not to disrupt the usual activities of the hospital. The structured questionnaires can be found in the Appendix.

Besides the nutrition interviews - as mentioned above - the biochemical measurement of the trace element selenium for evaluation of the nutrition status was used. Of course, blood for the selenium analysis was collected in an extra test-tube. The selenium content of total blood was analyzed in the service laboratory by *biosyn* Arzneimittel GmbH in Fellbach (Germany); it was specified in µg/l.

It was also arranged to involve people with no thyroid dysfunction to compare their thyroid data and blood selenium levels with those of the thyroid patients. Although blood of each subject for selenium analysis was taken, in the end not all blood samples could be used for the present study. So, the total number of suitable blood samples was 91: Among them there were 85 blood selenium values of thyroid patients and the remaining six blood samples were blood Se values of people with a healthy thyroid.

3.2. Blood determination

The determination of the blood selenium level was one of the main points of this study. According to literature, it is very controversial if selenium intake is reflected in the blood or not. Generally, for the comprehension of selenium intake and its consequence on the blood Se level, knowledge about the exact absorption of selenium in the gastrointestinal tract is very important.

3.2.1. Combination of the blood Se level and the FFQ

For a validation of the study a biomarker was used to determine the adequacy of determination of the individual selenium intake. Therefore the “Total Selenium Intake Score” (TSIS) that was determined by means of FFQ, was compared with the blood selenium level.
The review about the most qualified methods of the Se determination by Ashton et al. (2009) was very revealing. It was suggested that whole blood selenium is likely to be a useful biomarker. The most important fact was that it is additionally a marker of the long-term status. Thus, whole blood analysis was chosen for the subject’s selenium status determination. Whole blood-selenium also responds to the changes in Se intake [ELMADFA and LEITZMANN, 1998].

The analysis of blood and its components is the best method for the diagnosis of

deficient diseases, because it is relatively simple to obtain and its parameters generally have higher significance than others. As total blood and serum Se content can be influenced by the nutrition supply, they are principally possible for characterization of the selenium status, provided that there is no anemia or hypoproteinemia. The nutritive selenium supply influences the serum selenium concentration in a lesser way than the total blood Se concentration, mainly by higher daily selenium supply [OSTER, 1992]. This makes the whole blood Se determination more compatible in combination with the FFQ.

Selenium levels in whole blood have been shown to alter with the change of residence from a higher to a low selenium area. As blood Se levels very strongly vary in different countries but also within a country or a region different selenium levels in serum or total blood can be found. There is non official limiting value [OSTER, 1992] and that is why it was primarily planned to compare Se levels among the subjects themselves. Whole blood (but also serum) Se levels reflect the current Se status of the individual, and mean levels obtained within a region indicate a general level of supply [SAGER, 2006].

Generally, a long dated back period like the past months or even the past year has to be (detected) taken into account for the selenium intake because of the latency between exposition and indisposition. The serum selenium level of adults is reached at the age of about 20 years and is not subject to any day-time variations and any day-time dependent consumption as well [OSTER, 1992]. Thus, it was not important to collect blood at a special daytime or to consider any other important factors concerning blood collection.

3.2.2. Blood samples

Blood samples were collected and kept in special boxes, called *Ethylene-diamine tetra-acetic acid* (EDTA) blood test tubes. Therefore only about two mililiters of blood were used per patient. Each subject was furnished with a consecutive number to blind the EDTA test tubes. Then, in the laboratory, each tube had to be rotated several times and kept cool in the hospital's refrigerator till they were picked up by the scientific *biosyn* staff who took them unopened to Germany where the selenium analyzes were made.

The determination of the selenium concentration in whole blood was made using

graphite tube-atomic absorption spectroscopy (AAS). Thereby the solution which had to be tested got atomized at high temperature. The absorption of a light ray that was produced through an element-specific electrodeless lamp got measured. Generally, in the analyses of blood and serum, a combination of Pd/Mg nitrate allows the use of higher pyrolysis temperatures. The characteristic resonance line of selenium lies by 196.0nm.

So, unspecific extinctions got severed with the *Zeemann-underground correction*. The content of the test solution got detected by the extinction comparison which was created of the reference curve of the calibration standards.

3.2.2.1. Laboratory Equipments

The equipment, which was used for the selenium analyses in whole blood is mentioned below:

- Micro wave digestion device MarsXpress with adequate pressure digestion vessels, CEM
- Zeeman- Atomic Absorption Spectrometer Analyst 600; Perkin Elmer
- Labor compensator (=Laborwippe)
- Pipettes

3.2.2.2. Reagents

For determination of the selenium status in whole blood some reagents were used that are described now:

Reagents

- Seronorn^{TM} TraceElements Whole Blood, Level I, (SNVB I), Synlab; calibration-whole blood
- ClinCal-Whole Blood Calibrator, (ClinCal), Recipe; calibration-whole blood
- Seronorn^{TM} TraceElements Whole Blood, Level II, (SNVB II), Synlab; reference-whole blood
- Nitric acid 65% suprapur, e.g. Merck
- Hydrogen peroxide 30%, Ph.Eur., e.g. Merck
- Palladium-nitrate solution 10g/l $Pd(NO_3)_2$ in 15% HNO_3, e.g. Merck

- Magnesium-nitrate solution 10g/l $Mg(NO_3)_2$ in 17 % HNO_3, e.g. Merck
- Deionized water
- Argon for spectrometry, e.g. air liquid

Prepared solutions

- Hydrogen peroxide solution 16%
- 266ml hydrogen peroxide solution 30% refilled with deionized water to 500ml
- Palladium/Magnesium modifier:
- 250µl Palladium-nitrat solution and 25µl Magnesium-nitrat solution refilled to 10ml with deionized water

3.2.2.3. Method of selenium analysis

Hydrogen peroxide solution 16% was made up with 266ml of hydrogen-peroxide 30% and got filled up with destillated water up to 500ml. The second attaching solution palladium/magnesium modifier was made up with 250µl palladium-nitrate solution. Finally, the 25µl mg nitrate solution got filled up to 10ml with deionized water.

For preparation, the digestion of the calibration-, reference- and test-whole blood followed. In the pressure decomposition instrument 1ml of whole blood was mixed with 2.0ml nitric acid 65% and 2.0ml hydrogen peroxide 16%. Afterwards, a microwave decomposition was performed. After cooling, the digestion was shaken and then it was conveyed into a scintillation vial.

With this done, the measurement could be started. The selenium concentration of the calibration solution depends on the selenium content of the calibration of total blood that differs from charge to charge. That is why the concentration declarations of the calibration standards have to be calculated before measurement. It is calibrated in an area of about 0-40µg/l. The calibration solutions got attached into the autosampler vials from the microwave digestions of the whole blood-calibration. The calibration standards got placed into the autosampler with ascended concentrations. The microwave digestions of the total blood samples became measured undilutedly. In regular intervals the digestion of the reference total blood sample (SNVB II) got measured for checking purposes.

Then the interpretation followed. The selenium concentration of the reference-total

blood and the total blood samples were calculated with the help of a linear correlation, the *law of Lambert-Beer*, between the extinction of 196.0nm and the Se concentration.

3.3. Questionnaires

3.3.1. Food Frequency Questionnaire (FFQ)

The Total Selenium Intake Score (TSIS) is split into its calculation and the definition of the state of finding.

The FFQ was worked out for nutrition monitoring to find how much selenium a thyroid patient daily absorbs by foods. For the development of the FFQ some important points had to be considered. The method had to be easy to administer and nearly independent from food composition databases because of the big variations.

As already mentioned, there are variations in food composition data in different countries and even within an area. This makes the calculation of the Se intake very difficult because consequently the selenium declarations in nutrient content tables cannot be (very) exact. So, it is a problem to rely on food composition tables for estimating individual intakes. The problem is particularly serious when variations occur in staple or selenium core foods [REILLY, 1996]. But in this study it could be assigned by using food Se data of recent publications and when not possible, data from Austrian nutrient tables had to be preferred.

For the definition of the received Total Selenium Intake Score (TSIS), estimated selenium intakes from literature were used for comparisons. Generally, when the intake and the elimination are measured for a long term, the supply can be estimated. Correctly made *Duplicate Diet Studies* give a practice-oriented overview of the actual intake. The study made in 1991 showed the Austrian averaged supply of about 35.5µg/d that ranged from 24-48µg/d. Another determination showed the estimated range between 36 and 68µg/day [PFANNHAUSER, 1994 and WILPLINGER and PFANNHAUSER, 1997]. A further Austrian estimation resulted in the mean daily intake of 48µg within the range of 27–68µg/d [SAGER, 2005 and SAGER, 2006]. And the most up-to-date averaged selenium supply is about 37-68µg/day, which is indeed under the adequate supply [STÜCKLER et al., 2010].

3.3.1.1. Benefits of FFQ

A lot of advantages of the Food Frequency Questionnaire (FFQ) made the decision simple to use it for this research. Because the FFQ is generally used for the determination of the supply of specific nutrients by foods and food groups respectively this method is suitable for this study. The FFQ helps to find correlations between nutrition and health [SANTNER, 1992] and particularly here, it is used to analyze the Se absorption by foods of thyroid patients or healthy people. Although principally the FFQ can be filled in by interviewers or probands themselves, in this study all interviews were performed by the same person to receive standardized results.

With the FFQ, for instance, there is no temporally, physic and psychic exposure of the proband. Furthermore, it does not stress the interviewees and seasonal variations also are included. The computer supported analysis makes the FFQ cheaper and thus, it can be used for a big study population.

Generally, the FFQ is one of the most commonly used nutrition technique in epidemiologic studies to assess the common consumption of a person and to find possible correlations to the appearance of nutrition-dependent diseases. Furthermore, it is a direct nutrition investigation method and it determines the nutrition status, the nutritional requirement and also measures the back dated nutrition supply [OLTERSDORF, 1995] which is the most important advantage of this method. Responses of the FFQ are used to rank individuals within a population by their dietary habits and to determine usual food consumption patterns of individuals [FREISLING, 2007].

The principle of the FFQ is based on asking of consumption frequencies of special foods and beverages that are usually consumed and so, a person with high or low supply can be identified [EBNER, 2004]. To achieve better results, the amounts of the consumed foods also have to be estimated [HAJEK, 2000].
The FFQ is adequate for this research because people easier remember how often they ordinarily eat special foods than which food of a special meal they ate in the past [FREISLING, 2007]. So, the FFQ with the consumption frequency and the averaged amount of the selenium-rich food was developed.

3.3.1.2. Key food-method

Nevertheless, for the development of the FFQ both, se-rich foods and their actual Se contents were needed. By the selection of foods it was tried to represent a balanced nutrition. Attention was also paid to the fact that the selected foods are often consumed in the average Austrian population. It this way, it could be found which of those influence the Se status most.
It has to be considered that if there are changes in the supplementation of feedingstuffs in animals it also affects foods consumed by people. The used selenium contents in FFQ have to be replaced. The values of the selenium contents in Austrian foods have to be substituted to get the right results. The actually used selenium contents are correct and updated.

The used technique is based upon the *key food*-method. Here, foods are selected that add to 75% to the selenium intake. Literature was gleaned and useful sources saved.

Besides other literature sources, the study by Anke (2002) assisted with the selection *key foods* for the FFQ. He found that animal foods add to about 69% to the selenium demand of women and to 75% of men. According to this finding, animal foods are very important for this study and especially for the development of the FFQ. Polunin (2008) also described paranuts, whole-grain cereals, sun-flower seeds, seafruits, algae and meat as reliable selenium sources [POLUNIN, 2008] which was also largely taken into account. In contrast, vegetables only have a share in 30% and 23% respectively and thus, vegetables were not incorporated into the present study. All se-rich foods which are moreover mainly consumed in Austria, were chosen.

The selected se-rich foods that additionally - according to the Food Nutrition Bulletin 2008 - are often consumed in Austria are shown in Table 17. This makes them the best selenium sources for the Austrian population. The main categories of the worked-out FFQ with the help of the *key food*-method are shown below.

1) Cereal and -products	1.1. Whole-grain 1.2. Wheat bread 1.3. Muesli
2) Nuts	2.1. Pistachio 2.2. Paranut
3) Animal products	3.1. Eggs 3.2. Poultry 3.3. Pork (incl. sausage) 3.4. Beef 3.5. Offal 3.6. Milk
4) Fish and seafruits	4.1. Freshwater fish 4.2. Shrimps 4.3. Sea fish
5) Pulses	5.1. Pulses (beans and lenses) 5.2. Soy and soy –products

Table 17: Selected foods for the FFQ

The main problem was to get suitable lists with Austrian values of selenium contents in foods. Even the Institute of Nutrition in Vienna still does not have any data of selenium supply. So, it was very difficult to rank foods relating to the importance as selenium sources.

Although the *Federal Food Key* (*BLS*) was developed as a standard instrument for the evaluation of epidemiologic nutrition studies and consumption investigation in the Federal Republic Germany, it does not contain any selenium values. And that is why the usual nutrition databases could not be used for the selenium calculation because they are based upon the German *BLS*. Therefore, the search for more actual studies and publications in which the Austrian Se concentrations in foods were determined began.

The selection of the foods mostly consumed in Austria is in agreement with the research results of the Austrian Environment Ministry [BMLFUW, 2010].

3.3.1.3. Selection of selenium-rich foods

After the selection of the single foods the selenium contents had to be found.

In spite of the large variations, there exist values of Se contents of different foods, nevertheless. The food composition tables like the GU Nutritional tables by Elmadfa and Leitzmann (1998) or the *Souci-Fachmann-Kraut-database* usually provide useful

information regarding the average concentrations of nutrients in various kinds of foods [STOJANOVIC, 2000]. These values were only used when a topical study could not be found. So, the used information about the selenium contents of special foods were searched from Austrian food lists but largely from ongoing studies. In this way, the single foods with their analyses of more precisely and up-dated Se contents were picked out from literature.

After receiving all the used data, the selected foods were listed in an Excel data sheet to compile the FFQ. The single food groups are explained in detail in the following lines.

First of all, the group of cereal and -products were examined to find foods that largely contribute to the selenium supply of the Austrian population. The main point to incorporate cereals into the questionnaire was that in Austria these foods are eaten very frequently. It is difficult to determine exact Se values because they do not depend on the sort or soil concentration and vary from year to year [SAGER, 2005] but nevertheless the amounts are determined. Although it is known from literature that wheat or cereals contain a lot of selenium, this is not correct any more today because in the past, cereals were mostly imported from North America to Austria [REILLY, 1996] and in contrast to our regions, in North America cereal products are the second most important selenikum sources [Bundesinstitut für Risikobewertung, 2004]. Today, Austria is a self-supporter concerning cereals and thus, Austrian cereals only show medial selenium contents [STOJANOVIC, 2000] because it is not allowed to fertilize soils with selenium-containing mixtures.
Nevertheless, bread is part of staple foods in Austria and this makes bread necessary for the FFQ. Bread was categorised into whole-grain and wheat bread because there are (small) differences.
Sager (2005) made a comprehensive screening of Austrian cereal samples from 1992-1994. For (winter) wheat he found a median of 0.027mg/kg, which was the most up-to-date determination and so it was used in the FFQ. Even though the actual content of wheat per unit weight is not very high, its frequency and the quantity of consumption is sufficient to make it a major source of the element for a lot of people [REILLY, 1996].

Because of outdated Austrian whole-grain bread data the actual value of 2 µg/100g by Rieger (2009) was used, although it did not show very big differentiations to the white bread Se content.

Rice and noodles, which also are part of the cereals food group, were excluded because no current selenium values could be found. Apart from that, noodles are also included in the category of eggs. Although in Austria the self-sufficiency of rice is 0%, it would be very difficult to determine its correct selenium content. For that reason, countries of origin had to be known and that was impossible. Although imported rice contains higher Se amounts [SAGER, 2006], it is relatively not eaten very often by the Austrian population [ELMADFA et al., 2009]. Furthermore, rice gives an extreme example of inter-country variations of selenium contents. For instance, rice from an area of high soil selenium in China was reported to contain up to 1.0µg/g of the element. Rice grown in Thailand contained 0.04µg/g, while in low selenium New Zealand a level of 0.02µg/g was found. So a 50-fold variation between the upper and lowest figures is given [REILLY, 1996]. Finally, muesli was also seen as a possible selenium source because some people eat it daily. The Se content was taken from a determination by Sager (2006) that is 0.024mg/kg.

The second groups were nuts and seeds which are rich in proteins, besides possessing big amounts of high-quality oils, essential vitamins, minerals and fibers. That is why they also rank among selenium sources. Generally, all foods that have a high content of amino acids are canditates for selenium accumulation. The label “nuts” is the usual collective name for walnuts, hazelnuts, almonds, chestnuts, pistachios, pecans, paranuts, cashews, and coconuts. But this graduation does not match the botanical classification, because, e.g., pistachios are stone fruits, peanuts are pulses, and paranuts are capsules. Nuts grow on se-rich soils and so they show a good se-accumulation. Pistachios and paranuts were picked out for the questionnaire because they come mainly from a very closely limited region and grow on high se-soil habitats like the rain forests. Pistachios are native in Iran and Syria and today they are mainly grown in South Europe and North Africa. For instance, the main suppliers for the German market are Iran and California [WEBER, 1999]. That is why pistachios are incorporated into the FFQ.
Some studies affirm the decision to choose them for the FFQ because common results showed that these are one of the best Se sources. According to the food-

data-base of the US Department of Agriculture (USDA) 100g Brazil nuts contain about 1917µg selenium and with one nut about 70-90µg selenium are absorbed. In Austria, Brazil nuts are only components of nut mixes. That is why Brazil nuts have a subordinated role in the Western nutrition [SIMONOVA and PFANNHAUSER, 2008 and Bundesinstitut für Risikobewertung, 2004]. Paranuts are to be found in *Studentenfutter* but in very low amounts and that is why for the calculation only the averaged amount of 5g was taken but they are important because of their high Se contents. Thus, both paranuts and pistachios were included into the FFQ because of their high selenium contents. These Se contents were taken from the calory fibula by Kiefer and Kunze (2008).
The consumption of seeds was not asked because - apart from the relatively low consumption - they mainly grow on se-poor Austrian soils.

The third group comprises animal products including meat, milk and eggs. Meat is classified pork, beef, veal, poultry and offal, which are the most common varieties on the Austrian market. Although meat is the most important selenium source for the human being selenium is not contained naturally because it has its roots in the supplementation of the animal feedingstuffs. Consequently, this also caused higher Se contents in milk and hens' eggs but also offal (kidneys, liver) [ANKE et al., 2002]. The selenium concentrations of meat were taken from the very topical study by Stückler et al. (2010). Although these determinations were made from raw meat, they could be used without any losses by cooking because according to literature there are no losses during preparation. The selenium-rich cooking waters are also consumed with meat as gravy or meat juices. Generally, all kinds of meat differ statistically significantly from each other in fresh meat and dry mass. Poultry showed the highest Se concentration, followed by pork, with beef showing the lowest contents. Regarding different quality programmes of production, selenium concentrations in beef varied between 58 and 96µg/kg, while in pork only between 147 and 162µg/kg. Poultry meat, derived from different major regions of Austrian production, differed slightly in mean selenium concentration. Chicken alternates from 159-175µg/kg and turkey from 119-138µg/kg which does not apply for beef and pork [STÜCKLER et al., 2010]. From here, the mean values of meat were taken for the calculation in the FFQ. Even Oster (1992) came to the same results and this was another positive factor for the application of these data.

In an international comparison a considerable accordance in the selenium content of eggs could be found, which - in contrast to other foods - is very high. The cause is that the feeding is a relatively normed method and it is allowed to add selenite and selenate to chicken feed [OSTER, 1992].

In Austria, the consumption of chicken eggs is very frequent, which makes eggs important Se sources, especially for lacto-vegetarians. About 236 eggs are consumed per person and year, inclusive egg concealed in different foods like bakery products or pasta. Laguna-Paredes and Sager (2010) made a determination of Austrian chicken eggs. Egg yolk (phosphor and calcium) and -white (sodium and sulfur) have different compounds. The selenium concentrations are definitively distributed normally. The selenium content of eggs is about 8.96±3.07µg, the mean range is 6.43µg in yolk and 1.89µg in egg white [SAGER and LAGUNA-PAREDES, 2010]. The selenium content in yolk is in the area of liver and higher than of fishes, as described by Oster (1992) in his research. An egg also covers the $^{1}/_{6}$ of the daily demand, which is 20-100µg selenium as daily demand for the human being [SAGER, 2010]. According to the estimations presented in the GU Nutrition Tables, the mean content of selenium in the entire egg is about 20µg/100g. A further analysis was made by Stojanovic. No significant differences in the Se content in commercially available eggs in Austria could be found, even when the type of chicken feed and different types of living conditions were taken into consideration.

These studies which showed very similar results, made the chicken egg indispensable as an essential Se source. Thus, the consumption of eggs was asked in this research too. Table 18 presents the Se content of commercially available eggs.

TYPE OF EGGS	Ca mg/100g	Fe mg/100g	Zn mg/100g	Cu µg/100g	Mn µg/100g	Se µg/100g
Free-range/summer eggs (FS)	42 ±9	2,2 ± 0,5	1,7 ±0,4	74 ±30	38 ±10	14,9 ± 3,9
Free range/winter eggs (FW)	37 ±8	1,6±0,2	1,2 ±0,3	50 ±14	20 ±6	14,5 ± 3,9
Flour system eggs (BoH)						
Four-grain eggs (BV)	33 ±4	1,7 ±0,3	1,5 ±0,3	39 ±16	18 ±4	13,6 ± 2,3
Battery system eggs (BAT)	29 ±4	1,8 ± 0,4	1,3 ±0,4	56 ±16	17 ±3	11,8 ±2,8
Docosahexaenoic acid eggs (DHA)	29 ±9	1,5 ±0,4	1,2 ±0,3	40 ±16	17 ±5	16,8 ±4,5
	29 ±7	1,8 ±0,4	1,15±0,3	30 ±10	23 ±6	13,9 ±3,4

Free-range/summer eggs – (FS)
Free-range/winter eggs - (FW)
Flour system eggs (BoH)
Four-grain eggs (BV)
Battery system eggs (BAT)
Docosahexaenoic acid eggs (DHA)

Table 18: Selenium contents of eggs [STOJANOVIC, 2000]

An average value from the different kinds of the commercial methods of the egg production was calculated because it was not traceable which kinds of eggs were eaten by the subjects. So, the used average value was about 14.3µg/100g.
For offal also the data by Rieger (2009) was used, in particular, 60µg selenium/100g offal.
There is only little information about the selenium content of cow milk. Rysavy et al. (2008) analyzed the selenium contents of milk from nine European countries which showed big variations. The highest average content of selenium was in samples from the Czech Republic and Slovakia. The lowest average concentrations were found in samples from Poland. The highest selenium contents were shown in the milk samples of the Czech Republic (45µg/l) and Slovakia (44µg/l), followed by Austria (35µg/l), England (33µg/l) and France (28µg/l). The determined packages were “Die leichte Muh Frühstückmilch” with about 16µg/l,” Ja! Natürlich Halbfett Milch” with about 75µg/l and “NÖM Fasten Milch” with about 13µg/l selenium. Milk makes a very good contribution to the selenium and iodine supply [RYSAVA et al., 2008]. The calculated milk Se value by Rysava was used for this study because it was the most recent determination of Austrian milk samples. So, milk, eggs, beef, poultry and pork were part of the FFQ.

The fourth group are fish and seafood that also have high selenium contents. Although there has been higher fish consumption (150g/portion) since 2001, fish plays a minor part in Austrian nutrition. But apart from that, fish consumption was

monitored because it also contains iodine and its interaction with selenium is very significant.

The fish demand is mainly covered by import and so the amount of local freshwaterfish is considerably lower than imported seafish [Österreichischer Ernährungsbericht, 2008]. Se is solved in seawater and so higher Se values can be received but they do not vary very dramatically. As mentioned, selenium can only be found in proteins not in fat. To illustrate the point: low fat fishes are flatfish, codfish, coalfish, zander and tench. Fishes with a high fat content are herring, mackerel and salmon. Codfish contains more selenium than herring in dry substance because herring is a very fatty fish. The selenium content of herring is about 210µg and that of plaice about 97.5µg/150g [KIEFER and KUNZE, 2008]. Nevertheless, there are often only marginal differences of the Se contents between fat-rich and fat-poor fish types. For the averaged portion size of fish 150g was chosen. That is why both kinds of fish are asked separately. For freshwaterfish the value of 16µg/100g was taken by Stojanovic (2000) and for seafish a mean value of the most eaten types - 50µg/100g - was used.

As seafood is getting more and more popular in Austria, as part of the “Asia Wave”, shrimps were also included into the FFQ. Shrimps are consumed more often because they are more frequently on offer in supermarkets. There, they can be purchased as take-away food, as preserves, canned or from the refrigerator shelf [Österreichischer Ernährungsbericht, 2008]. The selenium level of shrimps was also chosen by the calculation by Kiefer and Kunze (2008), which is 41µg/100g.

In Austria, the consumption of pulses is not very high but generally, protein-rich leguminosae supply plenty of selenium to the food chain [ANKE et al., 2002]. Vegans and vegetarians eat cereal products, pulses or nuts more often than people who eat a mixed diet. The consumption of pulses has decreased continually since the 90ies. In 2006/07, the usage of pulses was about 0.3kg per head and year [Österreichischer Ernährungsbericht, 2008]. Despite the low consumption in Austria, they were also asked in the FFQ because they are such good protein sources. Furthermore, soy and soy products are grown in significantly larger amounts for people’s regular consumption. Normally, there is a difference in the selenium status between people who eat soy products and those who do not eat them. Special legumes like Azuki beans, red lentils, chickpeas, mungbeans and soybeans are mainly imported from North Africa, Mexico, India, Pakistan, Turkey, Italy and France [BIO AUSTRIA, 2006]

which explains the higher Se content. For this study, all kinds of lentils and beans have been summarized in the category pulses [Österreichischer Ernährungsbericht, 2008]. The mean value of the most eaten kinds of pulses was calculated, which is 16.5µg selenium/100g. Again, for soy, the values by Kiefer and Kunze (2008) could be taken.

The importance of fruits and vegetables for the selenium intake is very low. That is why they were not included into the analysis at all.
From 1988 until the end of the millenium, the selenium contents of vegetables were studied. The outcome was that they are generally poor in selenium. This applies to all foods rich in starch and sugar. But the exceptions are cruciferae, asparagus and mushrooms, which supply plenty of selenium to the food chain [ANKE et al., 2002].
It can be said that in Central Europe there is a low Se intake from vegetables. In Austria it is not allowed to fertilize crops with selenium-containing mixtures. Although lots of potatoes are consumed in Austria, they are no Se sources because they contain little amounts of proteins (polypeptides) which in turn show little amounts of se. In this case, even if potatoes grow on se-rich soils, selenium concentrations would stay low.

Summing up, for the calculation of selenium intake the food groups of cereals and -products, nuts, animal products, fish inclusive seafruits and pulses were chosen. So, subjects could be asked about their individual Se absorption with the help of these foods. The final version of the selected se-rich foods for the FFQ inclusive the actual Se contents and averaged portion sizes of Austrians are demonstrated in Table 19. All the values were taken from recent studies and Austrian food lists respectively. It also shows the references from which the Se values were finally used.

Food group	Literature	Amount/Φ portion size	
1) CEREALS		**se/100g**	**se/ serving size**
Wheat bread	[SAGER, 2005]	0.027mg/kg	1.62µg/**60g**
Whole-grain bread	[RIEGER, 2009]	2µg/100g	1.2 µg/**60g**
Mixed bread (Φ value)			1.41 µg/**60g**
Muesli	[SAGER, 2006]	0.024mg/kg	1.32g/55g
2) NUTS			
Pistachios	[KIEFER and KUNZE, 2008]	450µg	112.5µg/25g
Paranuts	[KIEFER and KUNZE, 2008]	100µg	5µg/5g
3) ANIMAL PRODUCTS			
Eggs	[STOJANOVIC, 2000]	14.3µg	8.6µg/60g
Poultry	[STÜCKLER et al., 2010]	14.8µg	18.5µg/125g
Pork (incl. sausage/ham)	[STÜCKLER et al., 2010]	15.5µg	19.4µg/125g
Beef	[STÜCKLER et al., 2010]	7.7µg	10µg/125g
Offal	[RIEGER, 2009]	60µg	75µg/125g
Milk	[RYSAVA et al., 2008]	**35**µg/l	9µg/ 250ml
4) FISH and SEAFOOD			
Freshwaterfish	[STOJANOVIC, 2000: Combs 1988]	16µg	24µg/150g
Shrimps	[KIEFER and KUNZE, 2008]	41µg	51.3µg/125g
Seafish (Φ value)	[RIEGER, 2009]	50µg	75µg/150g
5) PULSES			
Lentils	[KIEFER and KUNZE, 2008]	11µg	9.4µg/85 g
White bean	[ELMADFA and LEITZMAN, 1998]	**22**µg	19µg/85 g
Pulses (Φ value)		16.5µg	14.2µg/85 g
Soy and –products	[KIEFER and KUNZE, 2008]	60µg	51µg/85 g

Table 19: Selenium contents per averaged serving size

3.3.1.4. Evaluation of the selenium intake

A suitable method for the individual evaluation of the subject's Se intakes was developed. Table 20 shows the calculation method.

SIS	**=**	**Selenium concentration/ averaged portion**	*****	**Amount**	*****	**Frequency**

Table 20: Calculation of the Selenium Intake Score (SIS)

For the exact calculation of the selenium contents, first different foods were converted per averaged portion size of a meal. Therefore, the averaged portion sizes were taken from the Austrian Nutrition Bulletin 2008 and from the European Food Safety Authority (EFSA), which is the keystone of the European Union (EU) Risk Assessment regarding food and feed safety. The second step was to define the consumed amounts more exactly.
The individual portion sizes could only be measured indirectly with descriptions like the amounts used in households like a spoonful or by showing the usual serving sizes with fingers.

According to that, the consumption amount of each food was split into three groups: "1" for a normal, averaged portion, "1.25" for a medium and "1.5" for a big portion. So, the different food quantities could also be included into the determination. The last of the three factors was the consumption frequency. Therefore, the usual consumption frequency of single foods during the previous months was divided into nine categories. These were classified from never to more than once a day; all the factors are relating to one week. Each frequency category is demonstrated in Table 21.

Factor	Category	Definition
10	>1/day	More than once a day
7	1*/d	Once a day
4	>4*/week	More than four times a week
3	2-4*/w	Two to four times a week
1	1-2*/w	One to two times a week
0.5	2-4*/m	Two to four times a month
0.25	1*/m	Once a month
0.06	3-5 times a year	About three to five times a year
0	0	Never

Table 21: Categories of consumption frequency

For the exact calculation of the selenium intake, the Se concentration of the usual serving size was multiplied by the individual amount and then by its frequency. In this way the Selenium Intake Score (SIS) of each subject was calculated which led to the quantitative specification of the FFQ. Finally, the sum of each factor of the five food groups resulted in the Total Selenium Intake Score (TSIS).

3.3.2. Interviews

The interviews were carried out from Monday to Friday from 07:30 to 12:00 a.m. during hospital office hours. The questionings spanned a period of four months. Data were entered into the data file after the interviews were made so as not to distract patients during the interview. At the same time, all the data had to be coded for later analysis in SPSS.

Besides the FFQ, other special questions about nutrition were asked because a lot of factors influence the thyroid function. The used information about each subject could be divided into three groups, namely general data, common health and nutrition in particular. The individual data on health characteristics and diet habits were collected by interviewing the subjects. If patients could not answer detailed questions about his/her health status, like thyroid blood values, information was taken from the patients' card indices.

3.3.2.1. General and medical questions

General information about the subjects was obtained by recording their names, birthdates, weights and heights. For all the patients who reported their body measures, the Body Mass Index (BMI) was calculated. The BMI is the person's weight in kilograms divided by the square of height in meters. The BMI is a good measurement for the classification of overweight because of the close correlation between the BMI and the body fat content that is calculated from the body density [ELMADFA, 1998]. The BMI is divided into single categories from underweight to adipositas. According to Elmadfa (1998) the ideal BMI for men is from 20 to 25 and for women from 19 to 24kg/m^2. The actual classification by ÖGE that was also used in this study is presented in Table 22.

Classification	BMI (kg/m^2)
Underweight	**<18.5**
Normal weight	**18.5-24.9**
Overweight	**>25.0**
Obese	**25-29.9**
Adipositas I	**30-34.9**
Adipositas II	**35-39.9**
Adipositas III	**≥40**

Table 22: Body Mass Index chart [ÖGE, 2010]

According to Pschyrembel (1997), autoimmune diseases are mainly accumulating familially. The risk of developing a thyroid disease is greatest if there is a family history of it or of autoimmune diseases like rheumatoid arthritis or vitiligo. In this respect, it was asked if first or second relatives or none of them suffer from any thyroid dysfunctions. The duration of the existing thyroid disease and since how long the patient has been in treatment respectively, was asked. Furthermore, the subjects were categorisized into "1" for thyroid dysfunction and "0" for a healthy thyroid, which is neither hyper- or hypofunction nor any struma or thyroid cancer. One of the most important questions was about the type of the autoimmune disease of the thyroid gland like Hashimoto Thyroiditis (HT), Morbus Basedow and Thyroiditis de Quervain.

And this was additionally split into the status before and after treatment.

In periods of hormonal variance such as the perimenopause, menopause, pregnancy, or postpartum there is also a higher risk of developing thyroid diseases [SHOMON, 2004]. That is why even pregnant women were involved into the study. This question was divided into that about an actual pregnancy, the last delivery and if the woman suffers from PP thyroiditis. But also Oral Contraceptive Pills (OCPs) can influence the thyroid function and so, the intake of OCPs also was part of the interview.

According to the results of the sonography of each subject, echogenicity and struma nodosa but also the sum of the thyroid volume (right and left) was noted. As per results of scintigraphy, cold, warm and hot nodules are differentiated. Laboratory I and II included individual values of fT_3, fT_4, TSH, but also negative antibodies like a-TPO, TRAK and a-Tg. The status after thyroid operation was also asked to know if the patient had thyroid surgery, which of course has changing effects on his/her metabolism.

Generally, there is a correlation between chronic diseases and thyroid dysfunction [SHOMON, 2004]. I.e. patients with diabetes type I have a higher incidence of thyroid dysfunctions. Reversely, thyroid disease can trigger or worsen depression. Furthermore, thyroid disorders can lead to a change of the blood pressure and that is why hypertension is an important factor of this analysis too. An abnormal high cholesterol level may be an indicator of latent hypothyroidism. Some people even have levels of 300-500mg/dl, but they can go back to normal as soon as hypothyroidism is treated [SHOMON, 2002].
There was also asked if the patient had any kind of cancer in general to find more about the actual health status. Other diseases like colitis, rheuma and vitiligo were questioned because they also are in relation with the immune system. Hashimoto Thyroiditis patients are more often diagnosed with vitiligo than Basedow’s disease patients, for instance. Here, autoantibodies destroy the pigment building skin cells (melanocytes) and the disease patterns of vitiligo go along with a spontaneous incidence of a depigmentation. Total healing is possible in only limited cases [BRAUNSPERGER, 2004].
Furthermore, some diseases that are often caused by thyroid dysfunctions can influence the digestive system too. Thus, thyroid diseases can make people more

likely to get food allergies and food sensitivities like wheat, milk, cheese, or soy allergies. Allergies and sensitivities to particular foods or pathogens can cause inflammation in the intestinal system. They may also disrupt digestion, and ultimately leaky gut, which makes weight loss difficult. Inversely, inflammation occurs when a person still has a food allergy or sensitivity. Celiac disease, gluten intolerance and sensitivity are further known causes of thyroid abnormalities [SHOMON, 2004]. Also the existence of osteoporosis, metabolic diseases and chronic gastritis were part of the questionnaire. When the person is a smoker or he/she had a stomach infection or food poisoning in the past, especially bacteria *Yersinia enterocolitica*, there also exists a higher risk of thyroid dysfunction. Generally, an exposition to radiation, certain chemicals via water and food or through particular medical treatments or lithium can also develop a thyroid dysfunction [SHOMON, 2004] but these factors could not be analyzed.

There are some pharmaceuticals whose effects on the thyroid are already known. Among them, there are special antidepressants, especially lithium salts and some cardiacs. If a person has to take such drugs, there is a higher risk of hypothyroidism [SHOMON, 2002]. Interferon, a drug (aminoacid, cytokine) against hepatitis C, skin cancer, melanoma, or thrombophilia, but also amiodarone are known to impair the thyroid function and to induce an autoimmune thyroiditis. Moreover, amiodarone contains about 75mg iodine [TSANG and HOULDEN, 2009 and MIRZAEI, 2009].
Apart from that, the intake of thyroid hormones was also incorporated in the questionnaire.
The entire questionnaire is to be found in the Appendix, called “Questionnaire I – General and medical data”.

3.3.2.2. Nutritional habits

For the calculation of possible correlations between diet and thyroid (dys-) functions individual nutritional habits were asked which can be found in the Appendix “Questionnaire II- Nutritional habits” as well.

The change of the subject’s nutrition attitudes of the last months was incorporated in the questionnaire. As “feeding change” is a self-assessment of any changes in the person’s usual nutrition the results have to be considered subjectively. Possibly a change of the usual nutrition habit causes thyroid dysfunction or ameliorates thyroid

function. A fiber-rich nutrition accelerates digestion, yet in some people it also lowers absorption [SHOMON, 2002]. The compliance of different nutritional forms or special diets like vegetarianism was also part of the questionnaire because they may show interacting correlations to the thyroid function. Even unintended weight changes were asked because of an indication of general health problems. In relation to thyroid, hyperthyroidism often leads to weight loss and in contrast, hypothyroidism causes weight gain. According to self-assessment it was also asked if nutrition is more protein-, carbohydrate-rich or balanced.

The subject's general habit of eating iodine-containing foods - seafood, algae or fish - also needed to be found. If a patient has to eliminate iodine in his/her diet it means that the patient is not allowed to eat any foods or reduce eating foods that contain high amounts of iodine (because of his/her thyroid disease) according to the doctor's advice. Furthermore, the consumption frequency of fruits and vegetables but also of cabbage and soy and soy-products was included in the study. The number of used vegetable oils and the daily drinking amount of water or fruit juices was noted too in order to find possible correlations.

The frequency of the intake of stimulants including alcohol, especially beer was noted as well. Also people's coffee and tea drinking habits were noted. Even the consumption frequency of chocolate and chocolate-containing foods was part of the questionnaire. But also smoking habits and regular sport activities were not ignored in this context.

Based on literature data, most described selenium deficit symptoms were asked as to find connections to the selenium status. The main deficit symptoms are weight loss, constipation, depression, excitability, concentration disorders, low immunity, myopathies, fingernails changes like white marks or thinner and dull hair. According to Gärtner et al. (2002) namely, a low selenium intake is associated with a significant greater incidence of negative mood states and depressions [GÄRTNER et al., 2002]. But also hypo- and hyperthyroidism are coupled with psychic symptoms [FELDKAMP, 2010]. It is very interesting to see if the deficit symptoms really show any correlations to the actual Se level. The consumption of regional products and/or bio products was a further important factor for the selenium intake because of the selenium-poor soils in Austria.

Factors like infections, unbalanced diets, smoking, (excessive) alcohol consumption, and insufficient exercise contribute more to chronic diseases than a genetic disposition does [EBNER, 2004]. That is why all the (anamnesis-) questions were very important for this study.

3.4. Laboratory analyses and clinical parameters

Test results of the thyroid hormone status were used both from the latest determination and the day when blood sampling for selenium analysis was done. Latest thyroid values were used to compare changes after the possible treatment with thyroid pharmaceuticals, for instance.

Laboratory I values were taken from the patients' card indices and Laboratory II included the measurement of the most actual determination of the subjects. Thus, Lab II values were taken on the same day when also blood for the selenium determination was collected. Laboratory I describes the hormone status before and Laboratory II after the possible previous treatment. Patients who came for their thyroid determination the first time were listed in Lab II inclusive the values of the blood Se levels.

Generally, some tests are performed only once like by sonography. So, all data of the subjects were also entered into the Excel data sheet for later analysis.

3.4.1. Thyroid hormone blood parameters

Blood examinations give quantitative information about the thyroid hormone level and about the possible existence of antibodies. TSH and if necessary thyroid hormones always have to be determined to approve hyper- or hypothyroidism and the extent of a disruption of the thyroid's normal function. Examinations are made on clinical suspicion of a lack of or of elevated hormone production and with existing accordant symptoms. But they are also made when there is morphological abnormality of the thyroid [MEANS et. al., 1963].

A fine needle aspiration is made to determine if a nodule or a cyst is benign or malignant. Therefore tissue is taken with a very fine needle, which causes less pain than the conventional blood collection [MERCK, 2010]. Values of TSH, fT_4, fT_3, a-TPO, a-Tg and TRAK of each patient are determined dependent on suspicion of the type of thyroid dysfunction in general. These are the most important indicators to

describe the kind of thyroid dysfunction [MAZOKOPAKIS et. al., 2007]. Although normal ranges often differ in literature, this does not make any big differences in diagnostics. Table 23 shows an example of variations from the two hospitals the study population was picked out.

Thyroid parameter	**Reference range - *Wilhelminenspital***	**Thyroid parameter**	**Reference range - *Kaiserin Elisabeth Hospital***
fT_4	0.8-2.0ng/dl (ng%)	fT_4	0.9-1.9ng/dl (ng%)
fT_3	2.0-4.2pg/ml	fT_3	3.0-7.50pmol/l
TSH	0.3-3.5µU/ml	TSH	0.25-4.2µU/ml
a-TPO	0.0–50.0U/ml	a-TPO	0.0–63.0IU/ml
TRAK	0.0–10.0mU/ml	TRAK	0.3–1.75IU/l
a-Tg	0.0-200.0ng/ml	a-Tg	0.0–115.0IU/ml

Table 23: Reference values of thyroid parameters

TSH often is a very reliable coefficient because it affects the thyroid's growth and function [WISCHNEWSKI, 2005]. But even in the presence of normal TSH levels, the thyroid may be in the process of an autoimmune disease. The treatment with synthetic thyroxine for Hashimoto Thyroiditis (HT) parients can reduce the chance and severity of the progression of their autoimmune disease. Furthermore, it is able to stop the progression of Hashimoto's disease and it prevents the development of hypothyroidism [SHOMON, 2004]. The TSH levels categorized in different thyroid states according to the *Wilhelminenspital* are shown in Table 24.

Euthyroidism	0.3-3.5µU/ml	TSH normal
Hypothyroidism	> 3.5µU/ml	TSH increased
Hyperthyroidism	< 0.3µU/ml	TSH decreased

Table 24: Categorization of TSH

Generally, a determination of both fT_4 and fT_3 is made on suspicion of hyperthyroidism and it is necessary to determine only fT_4 if hypothyroidism is suspected [MIRZAEI, 2009]. Latent hypothyroidism is a mild form of hypothyroidism. Only the TSH value is augmented, depending on the iodine supply [SHOMON, 2004]. Table 25 shows the two forms of hypothyroidism and its main differences.

Apparent Hypothyroidism		Latent Hypothyroidism	
T_3	↓	T_3	in normal range
T_4	↓	T_4	in normal range
TSH	↑	TSH	↑

Table 25: Laboratory values of HT [BRAUNSPERGER, 2004]

The values of apparent and latent hyperthyroidism are indicated in Table 26.

Apparent Hyperthyroidism		Latent Hyperthyroidism	
T_3	↑	T_3	in normal range
T_4	↑	T_4	in normal range
TSH	↓	TSH	↓

Table 26: Laboratory values of Morbus Basedow [BRAUNSPERGER, 2004]

Thyreoperoxidase (TPO) is a membrane-bound glycoprotein and catalyses the oxidation of iodide-ions and the fitting of iodine into the tyrosine-rests of the Tg to T_3 and T_4. As of the almost complete binding of the thyroid hormones (T_3 and mainly T_4) in blood on three different proteins, thyroxin-binding globulin (TBG), thyroxin-binding prealbumin (TBPA) and thyroxin-binding albumin (TBA), quick elimination is avoided through the kidney. The a-TPO is targeted against the extracellular part of the thyroid

peroxidase [WISCHNEWSKI, 2005].

Negative antibodies are the negative measured antibodies like a-TPO, a-Tg and TRAK, according to each clinical situation. The existence of antibodies is an important indicator because elevated antibodies in blood indicate an autoimmune thyroid disease. The reference value of a-TPO is more than 50U/ml and of a-Tg less than 140U/ml. But a high concentration of the a-TPOs in serum does not give any advice on the severity or the process of the disease [PFANNENSTIEL and SALLER, 1992].
Anti-TPO is established as a sensitive tool for the detection of AITD (including HT), follow-up of the response to immunotherapy, and identification of cases at risk for AIDT [MAZOKOPAKIS et al., 2007]. These antibodies are present in high concentrations in the serum of most patients with thyroiditis, but some of them do not have any antibodies, and the same antibodies are detected in some subjects with values in normal range. There is also no proof that the antibodies are the cause of the thyroiditis, but it is possible that they are a secondary phenomenon [MEANS et. al., 1963]. TRAK is evidentiary for Grave's disease, although negative antibodies do not exclude it with certainty and an elevated level of a-TPO is an indicator for HT.
Generally, the presence of antibodies may generate symptoms and are predictive for thyroid problems.

As mentioned briefly before, a very difficult situation occurs when thyroid dysfunctions do not show up on standard thyroid blood tests, the so-called hormone resistance. Here, the body is capable of producing thyroid hormones, but nutritional and metabolic dysfunctions make tissues resistant to them. This situation is comparable to insulin resistance, where - although the body produces enough insulin - the body does not react. The reason is that cells become resistant to it and so the body loses its ability to respond. So, thyroid hormone resistance and conversion problems are very difficult to diagnose with blood tests [SHOMON, 2004]. Among the subjects tested, this problem did not occur, however.

Each patient gets individual information by the doctor about the exact medication according to the thyroid parameters in blood. For treatment, thyroid hormones (Thyrex®, Euthyrox®), thyreostatic medication (Favistan=Thiamazol), ^{131}Iodine or thyreoidectomy are given by medical staff, which also was involved in the present

research. But generally, if patients are not responsive to pharmaceuticals, a thyroid surgery is advised in certain cases.

3.4.2. Sonography

In sonography, the volume, position, form and the interior tissue structure of the thyroid gland is identified. Table 27 presents the upper norm limits of the thyroid volume corresponding to different stages of life.

Life stage	Upper limits of thyroid volume
6-year old	4ml
13-year old	8ml
15-18-year old	15ml
Adult woman	18ml
Adult men	25ml

Table 27: Upper limits of thyroid volume [PFANNENSTIEL and SALLER, 1992]

The echogenicity reflects the number and height of the thyroid follicles that depend on the colloid amount and their function status. The interior structure of the thyroid tissue is expressed by regarding the echogenicity like echo-normal, echo-poor and echo-rich. Furthermore, it also describes the homogeneity including the homogenous and inhomogeneous structure, which reflects the arrangement of the echo pattern. The exact classification of the echogenicity shows Table 28.

Echo-normal	Normal big follicles
Echo-poor	e.g. empty follicle, micro-follicular structures
Echo-rich	Macro-follicular structures
Echo-complex	Concurrently appearance of echo-rich, -poor, -normal sonicphenomenons in one structure, not exactly definable
Echo-free	Cysts (with dorsal sonic amplification)
Echo-close	Calcification (with dorsal sonic shadow)

Table 28: Classification of echogenicity [PFANNENSTIEL and SALLER, 1992; modified]

The sonographic description of the diagnostic findings of Hashimoto Thyroiditis can be a normal, atrophic or hypertrophic form of the thyroid. Characteristically, the thyroid shows a diffuse, little inhomogeneous low echogenecity. But if the thyroid shows a totally echo-normal internal structure, HT can be excluded [PFANNENSTIEL and SALLER, 1992].

Echogenicity, the amount of nodules and the sum of the thyroid volume (right and left) were used for the present study as well for putting them into relation with nutritional habits of thyroid patients.

3.4.3. Scintigraphy

With scintigraphy, the regional thyroid function is determined. The patient is injected with a very low amount of a radioactively marked substance like technetium pertechnetate (99m-Tc, radioactive half-life of six hours), which mainly gets stored in thyroid. Then, the emitted radiation gets recorded by a gamma camera and because of the short half-life of this radionuclide, it gets eliminated after one day. Negative health effects do not have to be suspected with this method. In scintigraphy, cold and hot nodules are differentiated. Thyroid hormones are produced uncontrolledly by the existence of hot nodules. In contrast, cold nodules are inactive and do not produce hormones any more. In some cases fluid-filled holes are built up, so-called cysts. The fluid often has to be removed by puncture if they become very big [MERCK, 2010]. The hot nodule is also called autonomous adenoma and can lead to thyroid hyperfunction. For the present study data of scintigraphy were also used. Normal and abnormal thyroid functions were differentiated but also if a cold, warm or hot nodule persisted.

3.5. Statistical methods

All patients' data were entered into two different Excel files, one for the medical and the second for the nutritional data, and then summarized into one Excel sheet.

Microsoft Office Excel Version 2007 was used for statistical analysis. Afterwards it was transported into the program software *Statistical Package for Social Science* (SPSS, V 11.5, SPSS Inc.) for *Windows*. All data were presented as means ± SD (standard derivations), unless otherwise indicated [SAKR et al., 2007].

The description of different variables was done by using univariate analysis.

Independent t-test was used for comparisons of quantitative variables between two groups. Generally, the t-test is a method for the examination of statistical hypothesis and it is calculated if a test statistic lies in the decline range of the student distribution.

Differences between groups are assessed by using analysis of variance (ANOVA; with subsequent pairwise comparisons using a Mann-Whitney U-test), which was appropriate for this statistical research. Thus, one way ANOVA is used for comparison in multiple groups and was also employed in this study. In this way, deviations between the mean values can be differentiated. *Bonferroni test* is used as a post Hoc-test for comparison between groups.

Pearson correlation is a measure of linear correlation and used for correlation between quantitative variables. For instance, if two variables are connected together in a strong relation, but the correlation is not linear, the correlation coefficient according to *Pearson* cannot be used. *Pearson correlations* are computed to show the unadjusted relation between suggested influencing factors and frequencies and to gain insight into possible multicollinearity. It is used to examine linear relationships between continuous variables, e.g. FFQ scores and plasma concentrations of the biochemical indicators.

A further statistical method used was the *Chi-square test*. It is used for the comparison of qualitative variables between groups. For tables with two lines and two columns *chi-square* is used to calculate the *Pearson-chi-square*. But if both table variables are quantitative, *chi-square* was used as the correlation test linear with linear.

P is the probability of finding differences by chance. Like for all statistical testing, a *p-value* of about less than 0.05 was considered significant in all comparisons ($p<0.05$). And because of this condition, the probability of getting this result by chance is less than 5%.

IV) RESULTS

4.1. Patients characteristics

For statistical analysis of the selenium status and the individual nutrition habits of thyroid patients 216 people (n=216) were incorporated in the study. The major part is female with about 83.3% (180 women) and 16.7% of the subjects are male (36 men). The mean age of the subjects is 51.6±17.0 and it ranges between 15 and 87 years. There is no correlation between age and blood selenium level (r=-0.007, p=0.9). From four subjects there were no data from the questionnaires because they had no time to stay longer for the interview or they forgot to come at all. That is why these people have been partially excluded from the analysis relating to their special diets. Thus, complete data - that is both medical and nutrition data including answers of the FFQ - could be received from 212 subjects.

Twenty-one of the 212 subjects do not have any thyroid dysfunctions, neither hyper-, nor hypofunction, nor struma, which suggests that 191 subjects are thyroid patients. From a subgroup of 91 people blood was taken and the Se content was analyzed. Among them, there are four people with no thyroid dysfunction. However, no other data of these two female subjects could be obtained and that is why they also have been excluded from the statistical analysis.

The Body Mass Index (BMI) of the subjects ranges from 16.8 to 45.5 with a mean of 26.3±5.0 [kg/m^2]. Mean BMI is not significantly different between female (26.3±5.2) and male (26.2±3.9) patients (p=0.9). Thus, the BMI according to sex shows no significant difference in mean BMI. Using one way ANOVA, BMI is not significantly different between patients with hypothyroidism, euthyroidism or hyperthyroidism (p=0.76).

In general, there is no significant difference in BMI between subjects with and without thyroid dysfunction (p=0.1). Patients with a thyroid disease have a mean weight of 72.6kg±15.0 compared with 70.0±14.6kg in patients with no thyroid disease (p=0.4).

Serum selenium level is 104.9±17µg/l in obese patients (BMI ≥ 25) and 103±16.4µg/l in non obese patients (p=0.6). It is not related to patient weight (r=0.09, p=0.3). The

scatter plot below shows the serum Se level and the BMI of the subjects. The image on the right is fit line superimposed.

A further factor that is analyzed in this study is about the correlation between unintentional weight change and thyroid function. Weight loss is more often seen in hyperthyroid patients (48.1%) than in euthyroid (25.9%) or hypothyroid patients (25.9%).

Blood selenium level is 99.9±6.4µg/l in patients who take OCPs compared to 104.2±17.7µg/l who do not take it (p=0.6). Daily TSIS per kilogram of body weight is 0.45±0.19 in patients who take OCPs compared to 0.47±0.24 in patients who do not take it (p=0.7).

Eight pregnant women are among the subjects and are included into the study as a subgroup. Pregnant women have a selenium level of 96.1±9.4µg/l and the other female group 104.3±17.9µg/l. There is no significant difference in serum selenium level between pregnant and nonpregnant patients.

Other diseases, discomforts and the intake of special pharmaceuticals of the subjects are analyzed in this study too, naturally always in relation to the thyroid dysfunction. Free T_3 is higher (6.3±4.6) in patients with amiodarone or interferon intake than in patients (4.1±1.2) with no consumption of these two drugs (p=0.04). There is no significant difference in serum selenium level between patients who take drugs like Euthyrox or Thyrex and patients who do not take drugs. People who have to take one of these mentioned pharmaceuticals have a Se level of 103.2±16.3µg/l and subjects who do not have to take any have a level of 102.8±17.7µg/l (p=0.9). This is correct for each drug category as well (p>0.4).

Hypertension is seen in 20.5% of hypothyroidism, in 25.4% of hyperthyroidism and in 22.7% of euthyroid cases (p=0.8). Diabetes is noted in 5.1% of hypothyroid patients, 11.8% of euthyroid cases and 14.3% of hyperthyroid patients (p=0.3). Serum selenium level is 107.5±20.0µg/l in diabetic patients compared to 103.4±16.2µg/l in patients without diabetes (p=0.4). Hypothyroid, euthyroid and hyperthyroid patients have no metabolic disease or chronic gastritis in 92.3%, 87.3% and 81% respectively (p=0.3). Osteoporosis is seen in 7.7%, 6.4% and 6.3% of patients with hypothyroidism, euthyroidism and hyperthyroidism respectively (p=0.9).

4.2. Thyroid dysfunction

Regarding thyroid function, 51.9% of the total 216 patients are euthyroid, 29.6% are hyperthyroid and 18.5% are hypothyroid. 35% of all subjects have a kind of thyroid autoimmune disease as M. Basedow or HT. Five patients had thyroid cancer. However there is no significant difference (p=0.4).

Seven patients already had thyroid surgery. There is no significant difference in serum selenium level between patients with and without surgery. Subjects after an operation have a Se level of 100.6±24.3µg/l and subjects without it of 104.2±16.1µg/l (p=0.5).

Family history of thyroid disease is noted in 46.6% of the subjects. Thyroid dysfunction is noted in 52.3% of patients with familial thyroid dysfunction compared to 51.4% of patients with no family history of thyroid disorders (p=0.8). Serum selenium level is 104.3±19.2µg/l in these patients compared to 104.5±13.2µg/l in patients with no family history (p=0.9).

No correlation is noted between duration of thyroid disease and serum selenium level (p=0.5).

There is no significant difference between serum selenium level in patients with hyper- or hypothyreoidism (p>0.3). Sport activity and the consumption of fruits or vegetables is not different in these groups either (p>0.1).

The correlation of an existing autoimmune disease and the selenium level has been examined too. Blood selenium level is 104.9±16.0µg/l in patients with Hashimoto Thyroiditis and 106.7±12.1µg/l in patients with no autoimmune disease (p=0.6). Blood selenium level is 99.4±16.5µg/l in patients with Morbus Basedow and 106.7±12.1µg/l in patients without it (p=0.2).

In thyroid ultrasonography, normal echogenicity is noted in 50.2%, hypoechogenicity in 39.0% and hyperechogenicity in 5.2% of the subjects. 5.6% of patients have inhomogeneous echogenicity. Thyroid volume ranges from 2-120ml with a mean of 22.8±2.0ml. Sonographical thyroid volume and the number of thyroid nodules in ultrasonography is not related with serum Se level or TSIS (p>0.2). Thyroid volume is not significantly different in patients with hypo-, hyperthyroidism or in euthyroid subjects (p>0.2).

There is no significant difference in blood selenium level between patients with an enlarged thyroid compared to patients with a normal sized thyroid, neither with men nor with women. With women, the mean blood selenium level is 103.9±18.8µg/l with patients with larger volumes (>18ml) and 104.8±8.1µg/l with patients with ≤18ml of thyroid volume (p=0.8). With men, it is 104.1±12.2µg/l and 105.0±8.7µg/l with patients with a thyroid volume of >25ml and ≤25ml respectively (p=0.9).

There is no significant difference in serum Se level, daily Se intake and daily selenium intake per kg of body weight in patients with thyroid nodule on ultrasonography compared to patients with no nodule (p>0.1). Neither is a significant difference noted in TSIS, TSIS per kg of body weight and serum Se level between patients with single nodule or multinodular goiter (p>0.6).

Normal echogenicity is noted in 60.2% of euthyroid cases while it is seen in 31.6% of hypothyroid and in 46.0% of hyperthyroid patients (p=0.005). No significant difference in blood Se level, daily TSIS and daily TSIS per kg of body weight could be found with patients of different thyroid echogenicity either (p>0.3). The comparison was done between groups of echo-rich, echo-poor, heterogenous echo and normal echognicity of thyroid.

Blood selenium level was significantly higher in patients with cold nodules compared to patients with hot nodules. Mean blood selenium level is 115.2±18.7µg/l in patients with cold nodule, 111.6±5.2µg/l in patients with warm nodule and 93.2±14.7µg/l in patients with hot nodule (ANOVA, p=0.007). Using post Hoc analysis, patients with hot nodule had significantly lower blood selenium levels than patients with cold nodule (p=0.008). This is also true for a Selenium Intake Score per kilogram of body weight. SIS per kg of body weight is 0.53±0.25 in patients with cold nodule, 0.44±0.22 in patients with warm nodule and 0.37±0.13 in patients with hot nodule (p=0.04).

Changed eating habits are also crucial concerning the thyroid function. The difference between TSH levels of Laboratory I versus TSH of Laboratory II is 0.41 in patients with and 0.37 without food changes, which is not statistically different. It is either true for hypothyroid, hyperthyroid and euthyroid patients.

4.3. Nutritional habits and thyroid

All analyzes were made with the data of the thyroid state before treatment so as not to falsify results by the intake of drugs.

4.3.1. General nutrition and drinking habits plus sport activities

Among the 212 subjects, there are only two vegetarians and there are no other nutritional forms according to which people live.
Thyroid disease is present in 88.1% of regional product consumers compared to 98.1% of patients whose food is not dominantly derived from regional products (p=0.2). Mean blood Se level is 105.5±16.6µg/l compared to 102.6±16.7µg/l in patients with and without mainly regional product consumption (p=0.4).

Drinking amount has also been analyzed but there is no correlation between serum Se level and drinking amount.

Blood selenium level is 103.7±12.9µg/l in patients with a fairly protein-rich diet, 104.8±6.5µg/l in patients with carbohydrate-rich diet and 102.7±18.2µg/l in patients with a balanced diet (p=0.8), according to their self-assessment.

Generally, the consumption of different foods is a quantitative number. Thus, the amount of “0” means that there is no consumption of that food.
As all patients eat bread, no comparison between bread-eating and non bread-eating thyroid patients can be done.

Thyroid disease is seen in 86% of patients with and in 94.8% of patients without cereal consumption (p=0.02). The frequency of thyroid autoimmunity, thyroid dysfunction and thyroid cancer is not statistically different between patients who eat whole-grain bread compared to patients who eat wheat bread or both (p>0.4). Thyroid dysfunction, autoimmunity and thyroid cancer is not significantly different between groups with no consumption of muesli and daily, weekly or monthly consumption of it (p>0.1).
Even the frequency of thyroid autoimmunity, thyroid dysfunction and thyroid cancer is not statistically different between patients who regularly eat nuts and those who do not eat them regularly (p>0.1). Thyroid disease is seen in 90.5% of patients with and 89.8% of patients without nut consumption (p=0.8). The mean blood selenium level is

106.6±15.8 µg/l in patients with regular nut consumption and 101.2±17.1µg/l in patients who do not eat nuts regularly (p=0.1). Thyroid disease is seen in 90.8% of patients with and 89.4% of patients without pistachio consumption (p=0.8).
The same is true for consumption of pulses (p>0.2) because the mean blood selenium level is 104.6±16.7µg/l in patients with regular consumption of pulses and 93.1±11.8 µg/l in patients who do not eat pulses regularly (p=0.1). Thyroid disease is seen in 91.1% of patients with and 78.9% of patients without consumption of pulses (p=0.7).

The mean blood selenium level is significantly higher in patients who regularly eat meat (>4 times per week), which is 108.7±18.6µg/l, compared to patients who eat meat less frequently, which is 99.8±13.6µg/l (p=0.01). The frequency of thyroid autoimmunity, thyroid dysfunction and thyroid cancer is not statistically different between patients who eat meat regularly and those who do not eat it regularly (p>0.2). Autoimmune thyroid disease is noted in 35.8% of patients with regular meat consumption compared to 33.9% of patients without regular meat consumption (p=0.4). Thyroid disease is seen in 89.8% of patients with and 100% of patients without poultry consumption (p=0.5). Thyroid disease is also seen in 89.4% of patients with and 100% of patients without beef consumption (p=0.2).

Using Chi-Square test, there was no significant difference between people who eat more and less than four times a week meat respectively regarding hyperthyroidism, euthyroidism and hypothyroidism (p=0.4).

Euthyroid state is noted in 54.3% and 58.3% in patients with no or rare consumption of offal, while it is seen in only 24% of patients with monthly consumption of it (p=0.046). Thyroid disease is seen in 92.9% of patients with and 88.2% of patients without offal consumption (p=0.2). The mean blood selenium level is 102.1±19.6µg/l in patients with a monthly offal consumption and 104.3±16.0µg/l in patients with seldom or no consumption of offal (p=0.6).

The frequency of thyroid autoimmunity, thyroid dysfunction and thyroid cancer is not statistically different between patients who eat a minimum of 1-2 eggs per week and those who do not eat it (p>0.3). Thyroid disease is seen in 90.8% of patients with and 75% of patients without egg consumption (p=0.3). The mean blood selenium level is

104.8±14.4µg/l in patients with a minimum of 1-2 egg consumption per week and 102.6±19.4µg/l in patients who do not eat eggs regularly (p=0.1).

Only two patients did not drink milk. They were excluded from analysis. Blood selenium level is significantly higher in patients who drink milk daily (107.7±15.4µg/l) compared to patients who drink it weekly or monthly (94.5±15.7µg/l) (p=0.001).

The frequency of thyroid autoimmunity, thyroid dysfunction and thyroid cancer is not statistically different between patients who drink milk daily compared to patients who drink it weekly or monthly (p>0.1).
A “milk drinking factor” has been evolved for better analysis. Here, the frequency of milk drinking is multiplied by the averaged consumed amount: Using ANOVA analysis, the mean “milk factor” level is not significantly different between patients with and without thyroid disease (p=0.3). The milk factor is 2.05±1.2 in hypothyroid patients, 2.7±1.7 in euthyroid patients and 2.8±1.5 in hyperthyroid patients (p=0.051). Post Hoc analysis shows no significant difference between the different groups (p>0.06).

The general consumption of iodine-rich foods that includes fish, algae and seafood like shrimps and clams has been determined as well. From the 212 patients studied, 81 patients, who amount to 38.2%, eat iodine-rich foods routinely. It is seen in 41.0% of patients with hypothyroidsm, in 28.6% of patients with hyperthyroidism and in 42.7% of euthyroid people (p=0.1). Thyroid volume is 20.7±2.0ml in patients with consumption of iodine containing foods compared to 23.7±2.01ml in patients without them (p=0.3). Thyroid disease was seen in 90.5% of patients with and 83.3% of patients without regular fish consumption (p=0.3). Thyroid disease is seen in 92.7% of patients with and 83.3% of patients without fresh fish consumption (p=0.07). In contrast to that, thyroid disease is seen in 91.5% of patients with and 88.9% of patients without sea fish consumption (p=0.3).

Blood Se level is not different between subjects with regular fish consumption and people who do not eat fish regularly. The mean blood selenium level is not significantly different in patients who eat fish, which is 105.5±15.0µg/l, compared to patients who do not eat fish regularly, 102±18.3µg/l (p=0.3).

Thyroid disease is seen in 84.5% of patients with and 93.7% of patients without consumption of shrimps (p=0.03).

The consumption of fruits and vegetables is seen in 78.4% of patients with and 71.4% of patients without thyroid disease respectively (p=0.3). Blood Se level is 101.7±14.7µg/l in patients who routinely eat fruits, 107.1±19.3µg/l in patients who periodically eat vegetables, and 107.1±17.7µg/l in patients who eat both. In contrast to that, subjects who neither eat fruits nor vegetables have a Se level of 96.7±12.6µg/l (ANOVA, p=0.1).

The thyroid function relating to the consumption of goitrogenic foods is also examined. Regarding the consumption of cabbage, 90% of patients with thyroid disease and 71.4% of patients without thyroid disease eat it daily or weekly (p=0.04). Thyroid disease is also seen in 92% of patients with a monthly consumption of cabbage, in 91.8% of patients with daily consumption and in 76% of patients who do not eat cabbage (p=0.04). Mean thyroid volume is 14.3±8.0ml in patients with no cabbage consumption, increasing to 22.9±20.1ml in patients with a monthly consumption of cabbage and further increasing to 24.3±21.7ml in patients with daily or weekly consumption. ANOVA is used for this analysis (p=0.1). However, patients with daily or weekly cabbage consumption have larger thyroid volumes compared to patients with no consumption (p=0.002). Mean blood selenium level is 102.5±12.2µg/l in patients with a monthly consumption of cabbage, 106.0±20.1µg/l in patients with a daily consumption of it and 100.0±13.2µg/l in patients with no consumption of cabbage (p=0.4).

Thyroid disease is present in 76.0% of patients with iodine food consumption and no cabbage consumption, while it increases to 85.5% in patients with either iodine or cabbage consumption, further increasing to 96.4% in patients who eat cabbage and do not eat iodine (p=0.002).

Moreover, the consumption patterns of soy and soy products like tofu are determined. Thyroid disease is seen in 88.1% of patients with a consumption of soy products and 91.3% of patients who do not eat them (p=0.2). Thyroid volume is 21.8±21.9ml in patients who eat soy products compared to 23.1±18.9ml in patients with no soy product consumption (p=0.6). Mean selenium level is 109.2±19.7µg/l in patients who eat soy products compared with 100.3±13.2µg/l in patients who do not eat it (p=0.02).

Regular physical exercises are significantly higher in subjects with no thyroid disease compared with thyroid patients. Which means, that 57.1% of subjects without thyroid dysfunction do sports regularly, in contrast to 35.3% with thyroid disease who do not actively do sports regularly (p=0.04). About 35.9% of hypothyroid, 27% of hyperthyroid and 44.5% of euthyroid subjects have regular sport activities (p=0.07). However, the mean blood selenium level is 107.9±13.2µg/l and 102.2±17.7µg/l in patients with and without regular sports activities (p=0.1). Mean TSH, fT_3 and fT_4 levels are not different between patients with and without regular sport activity (p>0.1).

4.3.2. Subjects' stimulants intake

Thyroid disease is seen in 89.7% of patients who do not drink alcohol compared to 11.3%, 6.9% and 0% in patients who drink alcohol monthly, weekly and daily respectively (p=0.7). Euthyroidism is noted in 46.2% of patients who do not drink alcohol compared to 54.1%, 58.6% and 57.1% of patients who drink alcohol monthly, weekly and daily respectively (p=0.8). The mean blood selenium level is not significantly different in patients with or without alcohol consumption in general. People who drink alcohol have a Se level of 105.9±16.0µg/l and people who avoid alcohol have a level of 100.8±17.3µg/l (p=0.2).

Blood selenium level is 104.6±15.3µg/l and 103.4±17.4µg/l respectively in patients who drink beer or who do not (p=0.7). Euthyroidism is noted in 51.2% of beer drinking subjects and 52.3% of no beer drinkers (p=0.8).

Smoking is seen in 62.6% of patients with and 61.9% of patients without thyroid disease (p=0.8). No significant difference is noted in smoking between hypothyroid, euthyroid and hyperthyroid patients. 64.1% of hypothyroid, 61.9% of hyperthyroid and 61.8% of euthyroid patients are smokers (p=0.09). The level of anti-TPO, of anti-Tg and TRAK is not different in smokers and nonsmokers (p>0.5). Hyperthyroidism is seen in 22.6%, 55.6%, and 29.5% in patients who smoke, have discontinued smoking, and nonsmokers respectively. The mean blood selenium level is not significantly different in smokers compared to patients who do not smoke or have stopped smoking (ANOVA, p=0.3). The same is true for TSIS (ANOVA, p=0.8).

The correlation between the frequency of the subject's coffee consumption and the thyroid has been determined. As only three subjects drink more than five cups of

coffee daily, for a meaningful analysis, these have been thrown together with patients who drink three to five cups. Thyroid disease is seen in 11.4% of patients with daily fewer than or equal to two cups of coffee compared to 6.5% in patients who drink more than two cups (p=0.2). The frequency of different thyroid states is not different in patients who drink more than two cups of coffee compared to patients who drink fewer (p=0.5). Serum TSH, fT_3 and fT_4 is not different between patients who drink more than two cups a day compared to patients who drink fewer (p>0.6). The mean blood selenium level is lower in patients with fewer than two cups of coffee per day, namely 101.6±16.7µg/l compared to those who drink more, which is a blood level of 109.6±15.5µg/l (p=0.04).

The subject's tea drinking habit also is calculated. Mean blood selenium level is 102.8±16.3 and 108.3±17.3 in patients who drink tea or who do not respectively (p=0.2). Mean TSIS is not significantly different in these patient groups either (p=0.1).

Chocolate consumption is also included in this study in order to be able to see the relation of its ingredients to thyroid dysfunction. For better understanding it has to be mentioned that among chocolate consumption also chocolate-containing foods are included. A daily chocolate consumption is seen in 27.9% of patients with thyroid disease and 33.3% of patients without thyroid disease (p=0.3). It is also noted in 33.3% of patients with hypothyroidism and hyperthyroidism and 23.6% of euthyroid subjects (p=0.3). There is no significant difference regarding thyroid disease in patients with and without daily chocolate consumption (p=0.38). Mean TSH and fT_3 is not different between patients with daily consumption of chocolate and subjects who do not eat chocolate daily (p>0.4). Mean fT_3 is slightly lower, namely 1.3±0.2pg/ml, in patients with daily chocolate consumption compared to patients who do not eat chocolate or chocolate-containing foods daily. Contrastingly, the mean fT_3 level of the last mentioned group is 1.7±1.2pg/ml (p=0.03). The mean blood selenium level is 104.0±15.9µg/l and 103.9±17.5µg/l in patients with and without daily chocolate consumption (p=0.9).

4.4. Total Selenium Intake Score (TSIS) and blood Se level

The Selenium Intake Score (SIS) is calculated for each food category. These are cereals, nuts, animal products, fish and seafood and pulses. The single food groups only contain foods that are major Se sources of Austrian nutrition. The Selenium

Intake Score of each food category is not significantly different between patients with euthyroidism, hypothyroidism or hyperthyroidism ($p>0.1$).

The Total Selenium Intake Score (TSIS) is defined as the sum of SIS of all five food groups and then by adding up the selenium content per averaged quantity, serving size and the weekly intake frequency of each selenium-rich food. TSIS ranges from 48.0-574.2µg with a mean of 222.9±92.9µg selenium per week.

Besides TSIS, the Se blood level is determined to validate the results. A subgroup of 91 - 15 male and 76 female people - has delivered blood Se values but among them there are two people no other personnel or thyroid data could be obtained from. Furthermore, four of them have no thyroid disease and that is why they are excluded. So, workable data of 85 subjects remained. They underwent measurement of their blood selenium level ranging from 68.9-159.0µg/l. There is a significant correlation between selenium level and TSIS ($r=0.56$, $p<0.001$). Mean Total Selenium Intake Score is 232.0±94.6µg in patients with euthyroid state, 213.0±84.1µg in patients with hyperthyroidism, and 213.3±101.2µg in hypothyroid patients per week. Using *one way-ANOVA* there is no statistically significant difference in mean TSIS and different groups ($p=0.3$). According to this, the averaged amount of the daily absorbed selenium is about 33.1±13.5µg (range about 19.6-46.6µg) in euthyroid subjects, 30.4±12.0µg (18.4-42.4µg) in hyperthyroid and 30.4±14.5µg (15.9-44.9µg) in hypothyroid patients.

The blood selenium level is 104.1µg/l in male and 103.6µg/l in female patients ($p=0.8$).

TSIS per kg of body weight shows that the correlation coefficient is even smaller ($r=0.46$ vs. $r=-0.56$) when body weight normalized data are used. The selenium intake per kg of body weight or the daily intake is correlated with the blood selenium level. The same is true for the total selenium intake per week. The mean weekly TSIS is 219.0±81.4µg and 221.3±87.3µg respectively in patients with and without autoimmune thyroid diseases ($p=0.9$). According to this, the mean daily TSIS is about 31.3±11.6µg in patients with thyroid dysfunction and 31.6±12.5µg in subjects with a healthy thyroid. The same is also true for the blood selenium levels of 103.7±15.6µg/l and 106.7±12.2µg/l in patients with and without autoimmune diseases of thyroid respectively ($p=0.6$).

The mean blood selenium level is significantly different when comparing patients with different thyroid states. It is 94.8±13.4µg/l in patients with hypothyroidism, increasing to 103.2±17.4µg/l in hyperthyroid patients and further increasing to 108.4±15.9µg/l in euthyroid patients (p=0.013). Using Bonferroni test as post Hoc analysis, it is found that there is no significant difference in blood selenium level between euthyroid and hyperthyroid patients (p=0.58), while it is higher in euthyroid compared to hypothyroid subjects (p=0.01).

There is no correlation between fT_3 (p=0.68) or fT_4 (p=0.5) and blood selenium level. The serum TSH level is inversely correlated with the blood selenium level (r=-0.35, p=0.01).

The number of selenium deficiency symptoms is significantly and negatively correlated with the blood selenium level (r=-0.21, p=0.04).

This study also analyzes the correlation between fat consumption and the Se content in blood. Blood selenium level does not vary in patients who generally consume various types of vegetable oils (p=0.5). Subjects who consciously consume only one type of oil have a Se level of 104.5µg/l and people who consciously use more types have a level of 101.9µg/l.

An examination is also being made of the blood Se level and the TSIS of patients who first came for a thyroid examination and those were to be found in the Elisabeth Hospital (KES). But with those 38 patients, no correlations between blood selenium level and TSIS or daily TSIS per kg of body weight could be found. And so, no further inquiries of this subgroup were performed.

4.5. Case studies of patients supplemented with selenium

Case Study I

In 2004, Hashimoto Thyroiditis was diagnosed in the 39-year-old woman and she had to take thyroid specific drugs. These were the synthetic thyroid hormones *Euthyrox 50µg*, one tablet daily. She took the thyroid hormones till December 2007 because then her specialist in internal medicine advised her not to take them anymore.

Additionally, the patient received treatment by a homeopath. For a gynecological examination, she was referred to the Wilhelminenspital. She was diagnosed with subclinical hypothyroidism referring to chronic immunothyreopathy. Before introducing a substitution-therapy the gynecology department wanted to be sure.

In November 2008, she was referred to Dr. Mirzaei, the medical director of the Department of Nuclear Medicine of the Wilhelminenspital. The patient was 1.60 tall and weighed 51kg. Her thyroid volume right was 3.4ml, the left side was 2.8ml and it was echo-poor.

Because of her extremely high anti-TPO values, Dr. Mirzaei advised her to take selenium supplementations. Consequently, she talked to her homeopath. One day after the physical examination, the woman had surgery because of her ovary carcinoma, which of course affected her total immune system.

In February 2009, she had another examination in Wilhelminenspital. Her thyroid values were analyzed again because the day before (02.02.) her TSH was 2.46µU/ml. At that time she additionally took the combination preparation of 150µg selenium und vit ACE daily, as prescribed by her homeopath. She had to take one tablet of *Euthyrox 50µg.* Her thyroid volume was right 2.6ml and left 2ml (-> decrease of volume).

In June 2009, the thyroid patient made a determination of vitamins and trace elements in a laboratory in Vienna. There, her total blood selenium value was 159µg/l with a reference value of 80-130µg/l.

In August 2009, another examination of her thyroid was done, having continued taking SELENASE 200µg by Biosyn. Her a-TPO was a little bit higher than at the last examination but with a far lower result than the antibody values at the beginning of

her therapy without selenium. She also took *Euthyrox 50µg* (once a day), her weight was about 52kg and her appetite was normal.

The first examination in October 2009 showed a TSH of 19.97µU/ml. Therefore a second checkup was done. Some days later in October 2009 the a-TPO values increased again in spite of selenium supplementation. She still continued taking *Euthyrox 50µg* and in the morning she took SELENASE, half an hour later taking the thyroid drugs. She weighed 51kg and the 24 h EKG was normal.

In January 2010, at her next examination in Wilhelminenspital, her a-TPO values decreased again. She continued taking *Euthyrox 50µg.* Till September she had to take SELENASE before taking Euthyrox and so TSH increased. Since October, the patient took daily Euthyrox first and then the selenium supplementation. In December the TSH was 8µU/ml. Her weight was unstable. Thyroid volume was right 4ml, which is echo-rich, and left 2ml. In contrast to that, the left side was slightly echo-poor and inhomogeneous.

In June 2010, there was a further analysis of her thyroid values while still taking Euthyrox. At that time, however, the antibodies of the patient were not determined.

The patient's most recent examination was in December 14th in 2010. The woman has continued taking selenium for about two months.

Table 29 presents the course and change of thyroid values of the woman in a survey.

Date of examination (Case I)								
	Nov. 2008	**Feb. 2009**	**Aug. 2009**	**Oct. 2009**	**Jan. 2010**	**June 2010**	**Dec. 2010**	**Reference values**
fT_4	1.2	1.6	1.2	1.2	1.3	1.4		0.8-2.0ng/dl
TSH	8.2	2.1	1.8	19.3	5.7	1.5		0.3-3.0µU/ml
a-TPO	959	113	287	578	419		412	0.0-50U/ml
fT_3						1.9		2.0-4.2pg/ml
a-Tg							143	0-140ng/ml

Table 29: Changes of thyroid values of Case I

Case Study II:

In August 2010, Hashi-Toxikose was diagnosed in the 35-year old woman, a mother of two children. She had a suppressed TSH value with euthyroid parameters in periphery. Her basal TSH was 0.11µU/ml in August that year. Additionally anti-Tg and anti-TPO were positive although the woman did not have any thyroid-specific medical condition. The scintigram with 99m Technetium (Tc) showed that her thyroid is symmetrical and that there is a relative homogeneous Tc-uptake in both thyroid lobes. According to sonography, her thyroid is normal sized with low inhomogeneous structure and its total volume is 8ml. In the supplementary test with the Echodoppler the vascularisation of thyroid was not augmented.
With the help of a diet the patient reduced about 6kg weight (from 64.5 to 68 kg).

In October 2010, she was referred to the nuclear medicine department in the Wilhelminenspital from the urological department because of her positive values of a-Tg and a-TPO. She weighed 65kg (and she has two children). Her thyroid volume was 8ml and slightly inhomogeneous. She was advised to talk with her homeopath to take selenium too.

In November 2010, she had another examination. At that time she still took 200µg se, once a day. She then started with selenomethionine two times 100µg a day. For therapy, she had to continue taking 200µg of selenium daily, with a follow-up examination in 3 to 4 months. The taking of selenium showed a slight fall of a-Tg antibodies compared to the previous examination. This is demonstrated in Table 30.

Date of examination (Case II)			
	Oct. 2010	**Nov. 2010**	**Reference values**
fT_4	1.0	1.0	0.8-2.0**ng/dl**
TSH	2.0	2.0	0.3-3.0**µU/ml**
a-TPO	6.7	6.7	≤ 50U/ml
fT_3	3.0	3.0	2.0-4.2**pg/ml**
a-Tg	185	154	0-140**ng/ml**
TRAK	<2.5		0.0–10.0 mU/ ml

Table 30: Changes of thyroid values of Case II

V) DISCUSSION

The main objective of this study was to analyze the selenium intake of thyroid patients through foods by developing a Food Frequency Questionnaire (FFQ). The selenium-rich foods from the food list of the FFQ had to be part of the averaged Austrian nutrition as well for a comprehensive screening. For the more detailed calculation of the selenium intake, it had to include the quality and quantity of the absorbed selenium-containing foods. The food quality describes the kind of food. The quantity, however, is the averaged amount of a special kind of food people consume and its corresponding selenium content.

A further questionnaire was also generated for the present study to find possible correlations between the (dys-) function of the gland and diet.

Both, the dietary Se intake and the subjects' blood selenium levels were the main objectives. Also, parameters, like foods and special habits, were investigated to either enhance or decrease thyroid function and/or blood selenium level. The statistical analyzes provided very interesting findings.

5.1. Personnel data and thyroid (dys-) function of the subjects

5.1.1. Personnel data

5.1.1.1. Age, gender and weight of subjects

Test persons were randomly selected in the hospitals. For better comparisons with the thyroid patients, subjects with no thyroid disease were also incorporated into the study. The total of 212 persons provided a representative study population. Twenty-one subjects did not have any thyroid dysfunction, neither hyper- or hypofunction, nor morphologic abnormalities. Consequently, 191 of the test persons presented thyroid pathology.

Although in the beginning it was expected to select about 300 subjects for this study, finally there was a smaller amount of test persons because of some logistical shortcomings and because of patients who refused answering the nutrition questions. Anyway, the 212 subjects provide a representative study population for drawing valid conclusions.

The distribution of gender and age groups is demonstrated in Table 31.

Age	Total	%	Men	% men	Women	% women
≤20	4	1.9	0	0	4	100
21-40	54	25.5	5	9.3	49	90.7
41-60	84	39.6	15	17.9	69	82.1
61-80	61	28.8	14	23.0	47	77.0
≥81	9	4.2	2	22.2	7	77.8
Sum	212		36		176	

Table 31**:** Gender and age spreading of the subjects

The mean age of the subjects was about 50 years. The main part was female with 83% of the subjects.
It is generally known that women are respective for participating in nutrition interviews than men. However, this does not play an important role in this study because almost all people who were asked for being part of this study did not refuse, also males.
Furthermore, the high participation of women is in accordance with literature too. Mainly women are affected by thyroid malfunctions. Thus - as expected - the quantity of male test persons was quite low. This fact additionally affirms what the sample is indicating.

No correlations could be found between the age and the blood Se level, which is also very often described in literature. Swanson et al. (2008), for instance, found, that age is not associated with the tissue selenium content. In contrast to that, it was described that the selenium level of geriatric patients diminishes with age [RÜKGAUER et al., 2003]. In the present research – as already mentioned - the mean age of the subjects was about fifty years. But geriatric patients are much older than seventy. Maybe the decrease of the blood selenium content is only due to advanced age groups. Particularly, at an advanced age, there is a generally increased demand for antioxidants, like vitamin A, C and selenium. Akbaraly et al. (2007) found that the greater the decrease in plasma selenium, the higher is the probability of cognitive decline. It was also found that the selenium status decreases with age [AKBARALY et al., 2007]. Even in the study by Akbaraly et al. (2007), the mean age was higher than that of the present study. Thus, the age above sixty may

show an (age-dependent) decrease of the blood Se level. It can be assumed that people who are younger than sixty have blood selenium levels regardless of age.

Based on the knowledge that thyroid dysfunctions may contribute to involuntary weight changes, it was also examined. The BMI of the subjects ranged from 16.8-45.5 kg/m^2 with a mean of 26.3±5.0kg/m^2. The BMI was not significantly different between female and male subjects. As expected, each weight class was represented with a tendency to overweight. This accords with Elmadfa and Leitzmann (1998) because the ideal BMI values are not ever reached in Austria. The subjects' mean BMI was (slightly) above the normal range. Generally, the normal range spreads from 18.5-24.9kg/m^2. Overweight is defined as a BMI greater than 25.0kg/m^2. This demonstrates that most of the subjects were overweight and obese respectively. It also reflects the averaged Austrian population. The subjects' classification concerning the BMI but also the spreading of healthy test persons (marked gray) and thyroid patients are shown in Table 32.

Classification	**BMI (kg m^{-2})**	**Women (n)**			**Men (n)**			**Sum of patients**	
		Hyper-	**Eu-**	**Hypo-**	**Hyper-**	**Eu-**	**Hypo-**	**Women**	**men**
Underweight	Men <20 Women <19	1	2	3	1	0+1	0	6	1
Normal weight	Men 20-25 Women 19-24	18	21+11	12	5	4	2	51	11
Overweight	Men 25-30 Women 24-30	19	34+4	13	5	7+3	2	66	14
Adipositas	>30.00	11	18+2	7	4	2	0	36	6
Total	**Thyroid patients**	**49**	**75**	**35**	**15**	**13**	**4**		
	Healthy thyroid	**0**	**17**	**0**	**0**	**4**	**0**		

Table 32: Classification of subjects concerning BMI

Sixty-six female (19 hyper-, 34 eu-, and 13 hypothyroid) and 14 male patients (5 hyper-, 7 eu-, and 2 hypothyroid) were overweight. Furthermore, 36 women (11 hyper-/18 eu-/7 hypothyroid) and six men (4 hyper-/2 eu-/0 hypothyroid) of the thyroid patients were obese. In contrast to that, only seven people were underweight. Normal weight was seen in 62 subjects.
There is no significant difference in weight or BMI between thyroid patients and people without thyroid disease. This means that e.g. higher weight does not seem to be an indicator of thyroid disorders. Inversely, it is an indicator because thyroid imbalance may influence weight.

No significant differences between patients with hypothyroidism, euthyroidism, and hyperthyroidism concerning BMI could be found. Maybe some subjects did not know the latest state of their body weight. Anyway, there is a link between BMI and thyroid function because thyroid regulates the whole metabolism. Leitzmann and his team (2010) found that increased body size and physical inactivity are positively related to the risk of several cancers [LEITZMANN et al., 2010], for instance.

A further factor that is analyzed in this survey is about the correlation between the unintentional weight change and thyroid function. As expected, unknowing weight loss is more often seen in hyperthyroid patients than in euthyroid or hypothyroid people, which is caused by the elevated metabolism. This result is a proof for the validity of the subjects' statements. Hypothyroidism slows down metabolism and energy consumption, which demonstrates the link to weight changes too [SHOMON, 2004]. Only a small group of Hashimoto Thyroiditis patients suffer from underweight despite the thyroid hypofunction [HEUFELDER and BRAKEBUSCH, 2007]. Table 33 presents thyroid dysfunction concerning weight changes.

			Thyroid dysfunction-Thyroid state-before			Total
			Hypo-	Euthyroid	Hyperthyroid	
Weight change	No	Count	20	70	33	123
		% within Weight change	16.3%	56.9%	26.8%	100.0%
	Gain	Count	12	33	17	62
		% within Weight change	19.4%	53.2%	27.4%	100.0%
	Loss	Count	7	7	13	27
		% within Weight change	25.9%	25.9%	48.1%	100.0%
Total		Count	39	110	63	212
		% within Weight change	18.4%	51.9%	29.7%	100.0%

Table 33: Thyroid dysfunction and weight change

Involuntary weight loss is more often seen in hyperthyroid patients (48%) than in hypo- or euthyroid subjects (each about 26%). This is in accordance with the already known findings. Hyperthyroid patients - as already mentioned - lose weight more frequently because of their increased metabolism. In contrast to that, weight gain was more often seen in euthyroid people, followed by hyperthyroid and hypothyroid subjects. Furthermore, no weight change was mainly seen in euthyroid, followed by hyper- and then by hypothyroid subjects. About 57% of people with thyroid values in the normal range did not show any weight change. This is in accordance with literature too because an imbalance of thyroid hormones may cause weight changes.

The blood Se level was not related to the patients' weight although it was assumed that the higher the blood volume was, the higher was the Se content. The subjects' BMI in relation to the individual blood selenium levels is presented in Figure 14.

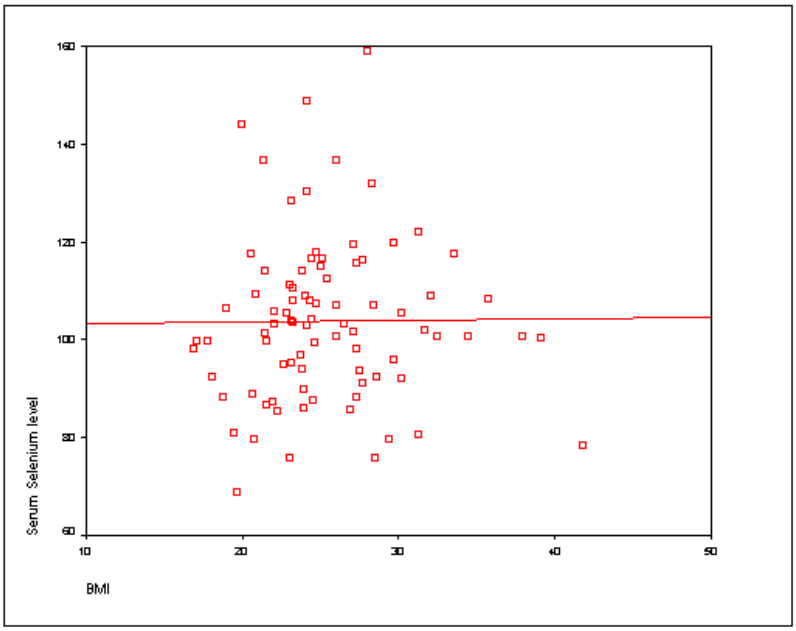


Figure 14: Blood Se levels and BMI

The plotted line shows very well that there is no correlation between the Body Mass Index and the selenium level in blood. Contrary to that, Ghayour-Mobarhan et al. (2008) could find a relation between weight and the selenium concentration in obese patients. They had significantly higher serum Se concentrations compared to non obese patients [GHAYOUR-MOBARHAN et al., 2008]. This showed again that it is possible that the subjects of the present study did not tell the truth about their weight because of a certain sense of shame or unknowingness. This, of course, falsified the result.

According to literature, obesity is frequently associated with modifications of the thyroid size and function. Hawkes and Keim (2003) found that serum T_3 decreased in the high selenium group and a subclinical hypothyroid response was induced. It led to body weight increases. In contrast to that, T_3 increased in the low selenium group and a subclinical hyperthyroid response led to body weight decreases. Thus, the dietary selenium intake modulates the thyroid hormone and energy metabolism in humans [HAWKES and KEIM, 2003]. Marras et al. (2010) and Shomon (2004) also found that there is a relation between weight and the T_3 level. Apart from that, Rafraf et al. (2008) investigated the serum selenium level in Iranian women. There it was affirmed that the serum selenium level did not vary with age and BMI [RAFRAF et al., 2008]. This is also in accordance with the present study.

5.1.1.2. Women of childbearing age

Only eight pregnant women were among the subjects. Their selenium levels were also analyzed because especially during pregnancy selenium plays an important role for the thyroid. Golubkina and Alfthan (2002) found that serum selenium concentrations of pregnant women in the former Soviet Union continuously decreased with advancing gestation. This also accords with Oster (1992), who noted that pregnant women in the last trimester have considerably lower selenium contents in serum and whole blood than at the beginning. According to Beckett and Arthur (2005), women with first-trimester miscarriages also have significantly lower serum selenium concentrations than in the first-trimester whose pregnancies went to term. In comparison with the recent result of the present study, no significant difference was found in the selenium level between pregnant and nonpregnant women. But the number of pregnant subjects was too low to get good and meaningful results. This analysis has to be made again with a higher number of pregnant subjects for better conclusions.

It is fairly well known that women who take contraceptives have a lower serum selenium concentration [GOLUBKINA and ALFTHAN, 2002]. This also proved true in the present study because the Se level in blood was (slightly) lower in women who take OCPs compared to women who do not. But this result was not statistically significant, most likely because of the low amount of subjects who take OCPs.
It is already known that the nutrient status (vitamin C, D_3, B_{12} and B_6) of women who take OCPs is very often conspicuously diminished. In those cases, the body is manipulated by synthetic hormones. So, it makes the organism work hard, which causes an increased need for essential nutrients [HAAS and LEVIN, 2006]. The high estrogen content augments the need for vitamin B_6 [FÄTH-NEUBAUER, 2008]. These women in particular have to consume nutrient-rich foods, including a selenium-rich diet.

5.1.2. Thyroid dysfunctions

The distribution of the varying kinds of thyroid dysfunction among the subjects must also be considered. About 52% of the total of 216 subjects was euthyroid, 30% hyperthyroid and 19% suffered from hypothyroidism. Thus, besides euthyroidism, most subjects were hyperthyroid.

35% of the study population had a kind of autoimmune disease, namely Morbus Basedow and HT respectively. Five subjects had thyroid cancer. Table 34 presents the spreading of the types of thyroid disorders.

Thyroid dysfunction	Women (n%)	Men (n%)	Sum (n%)
Hyperthyroidism	45 (78.9%)	12 (21.1%)	57 (29.8%)
Euthyroidism	74 (86.0%)	12 (14.0%)	86 (45.0%)
Hypothyroidism	35 (89.7%)	4 (10.3%)	39 (20.4%)
Thyroid cancer	3 (60%)	2 (40%)	5 (2.6%)
Thyroiditis deQuervain	2 (50%)	2 (50%)	4 (2.1%)
Sum	**159**	**32**	**191**

Table 34: Spreading of thyroid dysfunctions

The tabular representation above very well presents that especially women suffer from an under- or overactive gland, which accords with literature.
It should be born in mind that even thyroid patients can be euthyroid. Not all nodules produce thyroid hormones and so, normal thyroid values occur. In general, thyroid cancer and Thyroiditis de Quervain occur rarely and they did so among the study group.

The data showed that thyroid dysfunctions are more present in patients with a positive family history. When people know they have a higher risk, they can intensively deal with it by the right nutrition.
About half of the subjects present family history of thyroid disorders. It seems to indicate that there is a 50:50 chance to get a thyroid disease if there is a hereditary factor. It must be assumed that not all cases of thyroid diseases in the family were known. So, it is possible that there are many more patients with familial influences than could be ascertained.
Blood Se levels of the test persons did not differ between people with cases of thyroid disease among their first or second relatives and people without any family history of it. This shows that the blood selenium level depends on the individual Se absorption by nutrition. The whole blood selenium level does not seem to be dependent on the familial selenium status.

Attempting to find a correlation between the duration of the disease and the selenium level in blood was also one of the targets of this study. As expected, no correlation

could be found between the duration of the existence of thyroid diseases and the selenium level. There is no scientific significance because the duration of the disease depends on factors like education, availability of medical care and economic conditions. Thus, it cannot be related to the blood selenium level. This was verified again.

A comparison was also made between the thyroid function before and after treatment. Of course, euthyroid patients stayed euthyroid. From the forty hypothyroid subjects about half of them remained in the same status as before and the others got euthyroid. From the 64 patients with hyperthyroidism, 29 were afflicted by it even after treatment and four became hypothyroid. Neither is there a link between these changes and sports activity or the consumption of fruits and vegetables. It indicates that people eating a lot of fruits and vegetables, could not influence their thyroid functions negatively or positively. Maybe a much longer period of time is needed to see any changes.

5.1.2.1. Thyroid structure

Morphologic parameters of the gland were also used for analyzes. In thyroid ultrasonography, normal echogenicity was noted in about 50%, hypoechogenicity in 39% and hyperechogenicity in approximately 5% of the patients.

The thyroid volume ranged from 2-120ml with a mean of 22.8±2.0ml. It was not significantly different in patients with hypothyroidism, hyperthyroidism and euthyroid subjects. But this is a contradiction to literature. Normally, thyroid volume is smaller in hypothyroid states. This implies that there have to be differences between the thyroid states. Generally, the volume increases when there are inflammations or goiter formations. It also increases when – as already mentioned - there is an iodine deficit but in this study this could not be affirmed.

Sonographical thyroid volume and the number of thyroid nodules in ultrasonography were not related to the blood Se level or the TSIS. Thus, thyroid volume and the number of nodules do not seem to influence the whole blood selenium level. This also accords with Brauer et al. (2006). They also did not find any correlation between the thyroid volume and selenium level. But there was demonstrated that the thyroid volume is more correlated with iodine than with selenium [BRAUER et al., 2006]. Doupis et al. (2009) could also find no association between the selenium level and

the thyroid volume of Albanian people. With the latter findings, the mean thyroid volume ranged from 4.4 to 97.6ml and selenium levels from 30.6-138µg/l [DOUPIS et al., 2009]. For comparison, as the selenium levels in blood ranged from 68.9-159.0µg/l in the present research, generally speaking, it showed that the recent study population had obviously higher selenium levels than people in Albania. Thyroid volume was much higher in Austrian subjects as well.

As there was no significant difference in the blood selenium level between patients with enlarged thyroid compared to patients with normal sized thyroid, thyroid size does not influence the blood selenium level. Particularly, it was thought that an enlarged thyroid may also cause decreased selenium status. An enlarged thyroid namely often indicates that there is an iodine deficit. As iodine and selenium collaborate, they may be regarded as having an effect on the blood Se level.

5.1.2.2. Intake of thyroid drugs and other pharmaceuticals

With the actual study no significant differences in the blood selenium level between patients who take or do not take thyroid drugs like Euthyrox or Thyrex could be found. At this point special information has to be mentioned concerning the intake of thyroid hormones. Generally, thyroid hormone replacement drugs should not be taken within four hours of taking calcium or iron-containing supplements. Calcium can reduce the absorption, for instance. Thyroid drugs have to be taken on an empty stomach in the morning, about one hour before eating and around the same time each day. So, a maximum absorption and minimum interference with foods, dietary fibers, and supplements can be reached. The thyroid function should also be retested around six to eight weeks after dietary change or when a person starts or stops a high fiber diet. These can namely change the speed of thyroid drug absorption [SHOMON, 2004].

Thyroid was also regarded in relation to the intake of special pharmaceuticals. There is a high probability that people of advanced age have to take drugs. Free T_3 was higher in patients with amiodarone or interferon intake than in patients with no intake of one of these two drugs. Amiodarone partially blocks the used deiodases and so, it inhibits the conversion from fT_4 to fT_3. Generally, the ratio of T_4 to T_3 is affected by the iodine supply. But when there is any iodine deficit, the ratio changes in favor of T_3. It is well known that in the long-term, interferon leads to thyroid autoimmune disease [WEHNER, 2010]. As already mentioned, the intake of amiodarone or

interferon provides higher T_3 levels in patients' blood, which is in accordance with literature. It indicates that prescribed pharmaceuticals have negative effects on the thyroid function.

To come back to the study by Rükgauer et al. (2003), the selenium level of geriatric patients decreased with a higher amount of drug intake [RÜKGAUER et al., 2003]. In contrast to that, the selenium level, which is not influenced in the present study, is only related to the intake of thyroid drugs. Rükgauer et al. (2003) included other pharmaceuticals concerning the blood Se level as well. This seemed to make the difference.

5.1.2.3. Further diseases

There are also diseases that are in relation to thyroid function and vice versa.

Generally, arterial hypertension occurs when the blood values of an adult person are higher than 140/90mm Hg (systolic/diastolic). Typically, hypofunction leads to a higher diastolic and hyperfunction to a higher systolic value. It is known by now that hyperfunction may cause hypertension [ONMEDA, 2010 and SIMHOFER, 2007]. As expected, hypertension was more often found in people with hyperthyroidism and in diabetic patients. Although the study's outcome about hypertension is not statistically significant, it is nevertheless consistent with literature. With hyperthyroidism the whole metabolism is accelerated. But the data of this research are only based on subjects' statements and not on actual determinations of the blood pressure.
Hypercholesterolemia is defined as with all values higher than 200mg/dl (5.2mmol/l) but the exact values of the subjects could not be noted. The cholesterol level was only differentiated between elevated or not elevated. Maybe patients were not sure about their cholesterol levels and just said their assumptions, which of course made this analysis unusable. It would have been very interesting if the blood selenium level correlated with the cholesterol level in blood. In particular, several studies report that selenium absorption is strongly coupled with cholesterol-rich foods [OSTER, 1992 and BLEYS et al., 1993]. Maybe there is a correlation between the intake of cholesterol-rich foods and the blood selenium level of thyroid patients. But for significant conclusions, more detailed research is needed in this field.

Diabetes develops when the plasma glucose level (in blood) is higher than 7.80mmol/l. In this study, diabetes was mainly seen in hyperthyroid patients, followed

by euthyroid and then by hypothyroid subjects. But these results were not significant. The blood selenium level was 107.5±20.0µg/l in diabetic patients compared to 103.4±16.2µg/l in patients without it. Even so, this result is in accordance with the following study by Sager (2005). In principle, diabetes does not influence the Se level in blood but diabetics ingest more se-rich foods because of the advised protein-rich diet [SAGER, 2005]. Furthermore, an adequate diabetic diet additionally contains fewer sweets and fat. Thus, this diet significantly contains more selenium [SAGER, 2006]. This is another proof that general nutritional patterns influence the selenium status. This is why it was also asked if people eat a more protein- or carbohydrate-rich diet. To come back to the recent research, it was only found based on the patients' statements if they were diabetics or if they were not. Neither a tolerance test was made nor a differentiation between diabetes I and II. But according to literature, diabetes can be found more often in hypothyroid patients, which could not be proved in this study.

A further result - but not a significant one - was that hyperthyroid patients had a higher incidence of developing metabolic diseases or chronic gastritis. This also has to be better studied.

Osteoporosis was mainly reported by hypothyroid subjects. Apart from the insignificance of this result, osteoporosis is multifactorial because no medical data could be used either. Only the answers of the patients were noted and that is why this analysis is not further used, similarly to the question about diabetes. This is evidence for the fact that doctor's reports on their patients have to be used in order to be sure about proven medical anamnesis.

5.2. Dietary selenium intake and blood Se level of the thyroid patients

There are many reports in the literature regarding the essential role of selenium for thyroid. Selenium is needed to fight against a big number of free radicals, which are metabolic coproducts of the thyreoperoxidase function in the thyroid. If these protection systems fail, oxidative stress cannot be combated effectively and an increasing deletion of the thyreocytes appears. That is why the thyroid stores a very big amount of selenium [HEUFELDER, 2006 and AKBARALY et al., 2007]. Nutrition with a sufficient intake of Se is very important for thyroid health because it is able to

modify the immune response in patients with autoimmune thyroiditis [BECKETT and ARTHUR, 2005].

For calculation of the TSIS, the FFQ had to be evaluated. Generally, the memory is influenced by a lot of factors, like how nutrition is managed, the patients' interest in it, and other personal factors. Age and sex also are very important in this context. Women often have better memories than men, because they are often responsible for shopping and cooking [OLTERSDORF, 1995]. As most subjects of this study were female, it led to the condition that this problem could be held marginally.
If too many or too few questions about food stuffs in the FFQ were asked the subjects answered with a certain inaccuracy. Under- and over reporting are also possible mistakes in all questionnaires.

The difficulties in assessing the dietary nutrient intake argue for the use of biochemical markers. That is why the whole blood analysis of the individual selenium levels was chosen. Thus, the whole blood selenium determination was used for the long-term evaluation of the subjects' selenium intake, which was adapted to the FFQ.

5.2.1. TSIS

The Total Selenium Intake Score (TSIS) ranged from 48.0-574.2µg with a mean of 222.9±92.9µg selenium per week. The daily selenium intake equals exactly TSIS/7. Thus, the daily selenium intake ranged from 6.9-82.0µg with a mean of 31.8±13.3µg. Generally, it has to be born in mind, that a lot of factors, like the whole nutrition influences the selenium absorption. But in such a research, only the selenium intake could be considered.

Estimations about the optimal selenium intake are not coherent in literature. Thus, there will be taken a close look at some of the recommendations below.

In 1996, the WHO-estimated averaged daily intake of an Austrian person was 48µg [HATFIELD, 2001]. Considering the daily selenium intake of the thyroid patients of the recent research, there definitively can be noted a too low selenium supply.

According to the DGE, ÖGE, and SGE, the estimated value of the adequate selenium intake is about 30-70µg per day for adolescents and adults [DICKAU, 2009]. It almost completely complies with the estimations by Pfannhauser (1994) too. Thus, the mean range, which is 31.8±13.3µg, lies in the lower section of the reference range of the

ÖGE. This indicates that the general selenium intake of the subjects is quite low. In some cases there even is a too low daily selenium intake. Contrary, there is no risk for a too high daily Se intake because the UL is about 400µg [DGE et al., 2008].

In contrast to that, Oster (1992) described the mean value ranging from 16-70µg. According to this, the recent research of the mean Se intake does not show any drastic low Se supply. The levels were namely more above this minimum range. Nevertheless, the Se intake through foods should be heightened.

Another reference range is presented by Hatfields (2001), who defined the normative selenium intake for adult people with daily 30µg for women and 40µg for men. But in the present study no differences in the selenium intake between the two sexes could be found. Thus, it was compared with the recommendation for women because of their high presence in the study population. According to this, the mean range of 31.8±13.3µg generally accords with the female intake. But when considering it more detailed, it can also be noted a too low Se intake of some thyroid patients among the subjects.

According to the European Food Safety Authority (EFSA), the estimated nutrition-dependent selenium supply lies in the range of 24-89µg per day in the European population. For comparison, in Finland the intake is higher because of the selenium addition in agricultural fertilizers [AGUILAR et al., 2009]. This verifies that Austrian thyroid patients are not well supplied with the trace element selenium.

For a better definition, the Dietary Reference Intakes (DRI) was consulted too. Besides all other various reference values, the DRI is a good source for defining a subject’s selenium status correctly. With it, the proportion of test persons can be calculated who are below the so-called Estimated Average Requirement (EAR). The EAR is a daily amount of 45µg, which is used to examine the possibility of inadequacy of the reported intake. This makes it suitable information for the definition of the Se status. Among the 212 subjects, there were 183 people below the EAR. Thus, only 29 people were above it. Nevertheless, no meaningful differentiations between the Se intake below or rather above the EAR and people with thyroid dysfunction and without it respectively could be made. As there were many more thyroid patients among the subjects than healthy people, a definition of the Se supply in healthy subjects and people with thyroid disease was impossible.

It has to be kept in mind that all the data came from a cross-sectional study. Even if a correlation between the selenium intake and the thyroid disease is assumed, it is quite possible that the supply of the preceding year - as estimated by the FFQ - does not differ in both groups. The bioavailability between the groups may also be different. At this point, the blood selenium levels clarify the results. According to the present study, the mean blood selenium level was significantly different when comparing patients with different thyroid states. Contrary to that, the differentiation between healthy people and thyroid patients did not show any differences in the blood Se level. The blood selenium levels were only slightly higher in people without thyroid autoimmune diseases, but not significantly. Generally, although analyses of single nutrient intakes cannot be very exact in general, this problem concerns both groups after all. Thus, it shows special relations to each other nevertheless.

As shown, there are many literature sources with different reference areas. Nevertheless, a tendency to a deficit of the selenium intake through nutrition of thyroid patients was found. Literature namely shows higher reference values (or estimations) of an adequate selenium intake than the mean value of the study result does. Apart from that, the selenium intake of the subjects' range started at a daily Se intake of 6.9µg, which presented an extremely low daily Se supply of some patients.

Summing up, the present research showed that the dietary selenium intake of Austrian thyroid patients is quite low. Although the value of the TSIS was calculated from the whole study population, nevertheless, healthy subjects only account for 10% of the subjects.
Zimmermann and Köhrle (2002) noted that patients with destructive autoimmune diseases of the thyroid have an inadequate selenium supply. This is also proved by this research. The experts mentioned last also found that the senior population with no balanced nutrition and protein-poor diets has a low selenium status. Generally, it can be said that – according to the nutrition interviews – not all people consume prevailingly a balanced nutrition. Pulses and nuts, for instance, which both are important nutrient sources (especially of proteins), are not always consumed by the test persons. The fact that elderly people often have an inadequate Se supply is also reflected in this study. Among the subjects there were namely 31 people over the age of 70.

The selenium intake of thyroid patients and healthy subjects was also compared. The mean weekly TSIS was 219.0±81.4µg and 221.3±87.3µg respectively in patients with and without autoimmune thyroid disease. Obviously, it did not show the expectant significant difference.
As the daily Se intake ranged from 20 to 43µg in thyroid patients and from 19 to 44µg in people with a healthy thyroid, it illustrated the marginal difference between both groups. It seems that there is no difference in the Se intake between healthy subjects and thyroid patients. Thus, it is assumed that the bioavailability of the absorbed trace element selenium in the human body plays the most crucial part. According to some literature sources, with Grave's disease and Hashimoto Thyroiditis the selenium supply is increased [ÖGE, 2010]. It is also possible that - only mentioned in passing - no differences could be found because of inaccurate data of the subjects' answers by the FFQ.

The general low selenium supply of the recent study population in accordance with literature too. Stojanovic (2000) also noted that the nutrition status of the Austrian population is regarded to be low but still adequate. Austria is situated in the lower third in an international comparison [STOJANOVIC, 2000]. It resulted that there have been no changes concerning the Se intake of the Austrian people in the last years. As the body is able to adapt itself to the various selenium supplies in general [SIMONOVA and PFANNHAUSER, 2008], a lower Se status does not seem to be very critical. As reference values are also only estimations, it is not clear, if there is really a Se deficit in Austria or not. Of course, a slight augmentation would be good for fighting diseases, as lots of studies show.

The selenium intake of people with different thyroid states was also analyzed, which showed new findings. Mean weekly Total Selenium Intake Score was 232.0±94.6µg in subjects with euthyroid state, 213.0±84.1µg in patients with hyperthyroidism, and 213.3±101.2µg in hypothyroid patients. There was no statistically significant difference in the mean TSIS and both different groups of thyroid dysfunction. Nevertheless, it could be shown that euthyroid people have a generally higher whole blood selenium level than patients with hyper- and hypothyroidism. People with disorders of the gland generally seem to have a diminished Se status. It is also possible that there could not be found any significant difference because only about 19% of the test persons were hypothyroid and 29.6% of them were hyperthyroid.

Maybe a higher study population or rather an equally distributed number of the subgroups (euthyroid people and hyper- and hypothyroid patients) would have shown differences. It has to be remembered that the majority of the study population was euthyroid.

The Selenium Intake Score (SIS) from each food category was not significantly different between patients with euthyroidism, hypothyroidism, and hyperthyroidism. The absorption of selenium may play a significant role in this regards. Because of this result, the blood selenium level was consulted. The following diagram, Figure 15, shows the blood Se levels of the different thyroid states in comparison to the daily selenium intake.

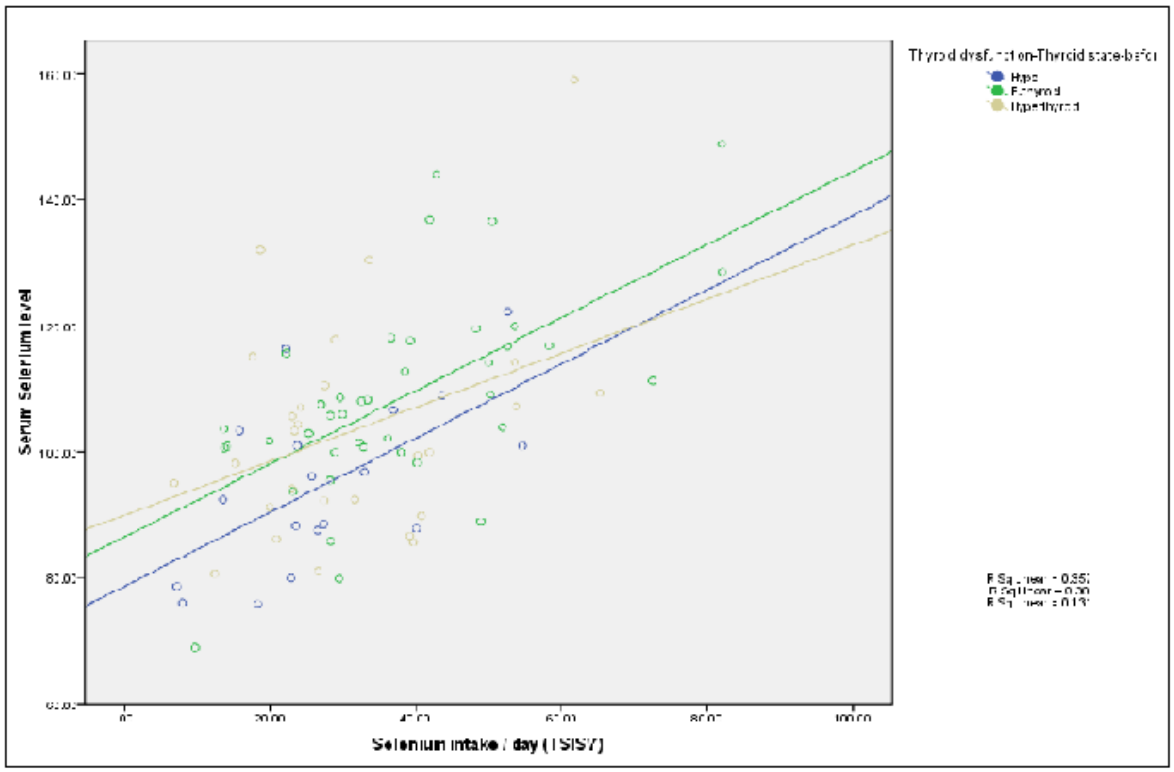


Figure 15: Selenium levels of different thyroid states relating to daily TSIS

Figure 15 shows that there is no significant difference between the three thyroid states and the Total Selenium Intake Score. But in spite of the outliers, a connection between the blood selenium level and the dietary selenium intake can be seen. The picture demonstrates very well that the higher the Se intake, the higher is the selenium level in total blood.

According to Longnecker et al. (1991), the selenium intake expressed per kilogram of body weight was more highly correlated with the blood selenium concentration than the absolute intake. Swanson et al. (2008) also found that the blood Se level was higher correlated to the Se intake per kg of body weight than the whole intake per day. Thus, it was also analyzed in the present study and it could also be evidenced. The correlation coefficient even was smaller when body weight normalized data were used. The TSIS was slightly higher in euthyroid subjects per kg of body weight. This supported the assumption that the TSIS per kg of body weight is a very interesting aspect in relation to the blood selenium level. The calculation of the individual selenium supply based on weight showed differences.

No significant difference was noted between the TSIS, TSIS per kg of body weight or the blood Se level and patients with single nodule or rather multinodular goiter. As nodules influence the thyroid hormone function, it was thought that the Se status is affected too. But the analysis did not show any meaningful correlation. Thus, selenium intake seemed to be independent from the development of nodules.

A further comparison was conducted between groups of echo-rich, echo-poor, heterogeneous and normal echogenicity of the thyroid. No significant differences in patients with different thyroid echogenicities were found either. Thus, according to the present study, echogenicity seems to be independent from the blood selenium level. The Se intake possibly does not influence the echogenicity either. Neither could be found any significant differences in the daily Se intake and the blood Se level in patients with thyroid nodule in general compared to patients with no nodule. This indicated that thyroid nodules do not influence the blood Se level.

The examination of the whole blood Se level and the TSIS of first-patients seemed to be interesting. These patients namely did not change anything concerning the intake of thyroid drugs. But with the 38 patients from the Elisabeth Hospital, no correlations

between the blood selenium level and the TSIS could be found. So, no more analyzes were performed from the subgroup of first-patients.

5.2.2. Blood selenium level

5.2.2.1. General blood selenium status

The subjects' blood selenium levels were among the main focus points of the present research. The comparison of the individual Se levels among each other was more important than the classification in reference areas. The reason for that is the difficulty to define exact reference values for the trace element selenium in human blood.
The blood selenium levels of eighty-five thyroid patients and of further four healthy subjects were incorporated into the study. Blood selenium levels ranged from 68.9-159.0µg/l.

Apart from the experts' discrepancies to define consistent reference values of the whole blood Se level, some of them are discussed now concerning the actual results. In 1992, Oster advised values of 73.2±12.7µg selenium/ l blood. Compared with the recent result, no Se deficit of the subjects was indicated. Table 35 presents further standard values of upper and lower limits of the total blood and serum selenium level.

Selenium		**Decreased**	**Optimal**	**Increased but clinically harmless**	**Control required**
Whole blood	**µg/l**	**<89**	**89-168**	**169-230**	**>230**
	µmol/l	<1.1	1.1-2.1	2.2-2.91	>2.91
Serum	µg/l	<74	74-139	140-190	>190
	µmol/l	<0.94	0.94-1.77	1.78-2.41	>2.41

Table 35: Reference values of selenium in whole blood and serum [WOLF, 2006 and WINNEFELD et al., 1995; modified]

As demonstrated in Table 35 there is reflected a deficit of the blood Se level in some subjects, however. As the lower limit is demonstrated with 89µg/l, the present study population shows with 68.9µg/l a decreased Se status in total blood. Contrary, the upper range lies in the optimal range. Again, - comparable with the daily Se intake - there is no danger of an increased selenium level in the subjects' blood.

Further reference values of the selenium status were published by the *German Environmental Federal Office* [UMWELTBUNDESAMT, 2002]. These are presented in Table 36.

	Selenium whole blood (µg/l)
Men	79-130
Women	60-120

Table 36**:** Reference values of blood selenium [UMWELTBUNDESAMT, 2002; modified]

As the *Umweltbundesamt* (2002) recommended a reference value in total blood for men of 79-130 and for women 60-120µg/l, it did not indicate a deficit in the recent study population of mainly female participants. Subjects' blood selenium levels, which ranged up to 159µg/l, showed even higher values than the upper limit of 120µg for women.

B*iosyn* also published standard values for the whole blood selenium level. Generally, the reference values greatly vary from year to year, which reflects the disagreement very well. The reference range by *biosyn* from 2009 indicates Table 37.

		Decreased	**Reference values (healthy people)**	**Starting toxicity**
Total-blood	**µg/l**	**<120**	**120-160[1)]**	**≥1087[3)]**
	µmol/l	<1.51	1.51-2.05[1)]	≥13.77[3)]
Serum	µg/l	<100	100-135[1)]	≥900[2)]
	µmol/l	<1.26	1.26- 1.71[1)]	≥11.4[3)]

[1)] Professional information by biosyn, [2)] [YANG et al., 1989], [3)] calculated of [1) + 2)]

Table 37: Reference values of blood selenium [biosyn, 2009]

In contrast to 2008, when biosyn recommended the optimal range between 100-140µg/l, in 2009 the reference values of healthy people were augmented to 120-160µg/l, as shown in Table 37. According to the recommendations from 2008, the lower limit of the present subjects was too low and the upper limit was even over the optimal range by *biosyn*. According to more recent recommendations by *biosyn*, the upper limit of the present subjects was in compliance with it. But the lower limit was considerably lower than the reference range. This showed again that there were

people with a very low selenium status among the subjects. It reflected people with thyroid disease in the study population.
Generally, an optimal selenium supply is given in countries like USA, Japan, the Middle East, and Switzerland with a total blood level of 120-160µg/l. Contrastingly, the selenium levels of a healthy German average population ranged from 53 to 65µg/l without taking any Se supplements [OSTER, 1992].

As often described in literature, diminished blood Se concentration is an indicator of the presence of diseases, in this case of thyroid dysfunctions. The decreased whole blood Se level very often shows that there is an imbalance in the human organism.

The general decreased blood selenium level of the subjects can be explained with the bigger number of thyroid patients among the test persons. Lower Se levels in people with different diseases were also found. This presents Table 38.

Disease	Selenium level (control)
Cancer (gastrointestinal)	0.0486 ± 0.015 (0.0543 ± 0.016)
Diabetes (children)	0.074 ± 0.008 (0.065 ± 0.008)
Myocardial infarction	0.055 ± 0.015 (0.078 ± 0.011)
Chron's disease	0.110 ± 0.036 (0.096 ± 0.035)
Alcoholic liver cirrhosis	0.058 ± 0.011 (0.080 ± 0.011)
Renal disease	0.078 ± 0.016 (0.103 ± 0.018)

Table 38: Plasma and serum selenium levels (µg/ml) in diseases [REILLY, 1996]

According to Table 38, the lowest Se level was seen in cancer, followed by myocardial infarction, alcoholic liver cirrhosis, followed by children with diabetes, renal disease and Crohn's disease. The lower limit of the recent study also showed similarly decreased blood Se levels (because the lower limit was 68.9µg/l).

The reduced blood selenium level in diseases was confirmed by further studies too. Clinical trials on patients with sepsis and systemic inflammatory response syndrome (SIRS) showed that they have low plasma selenium levels and low GPx activities [STREHL, 2006]. Sakr et al. (2007) also proved that selenium plays an important role in the defense against acute illness. In critically ill surgical patients, plasma selenium

concentrations were generally low [SAKR et al., 2007]. Rheuma patients have a lowered selenium level in blood as well [LOHMANN, 2008]. The effect of selenium or sodium-selenite in inflammatory rheumatoid diseases is primarily based on the anti-inflammatory and immune-modulating attributes. Special rheumatism drugs inhibit the glutathione peroxidase. They lead to a decrease of available selenium, which in itself leads to an amplification of oxidative stress [SILL-STEFFENS, 2003]. The plasma selenium level and the severity of rheumatoid arthritis show an inverse correlation [ELMADFA and LEITZMANN, 1998]. Table 39 gives an overview of blood selenium levels in different European countries. Furthermore, it shows the lowered blood Se levels in Viennese patients with benign mamma carcinoma.

Sample	Location	Mean selenium content (µg/l)
Human serum	Graz, Austria	64 ± 11
Human serum (20–60 years)	Zürich, Switzerland	90 ± 18
Human serum (60–100 years)	Zürich, Switzerland	88 ± 26
Whole blood	Southampton, UK	138 ± 19
Whole blood (fish-consumers)	Sweden	80
Whole blood (non-fish-consumers)	Sweden	91
Whole blood	Mainz, Germany	92 ± 18
Whole blood	Poland	101 ± 22
Whole blood	Ljubljana, Slovenia	88 ± 27
Whole blood	Central Italy	77
Whole blood	Northeast Italy	110
Whole blood	Vrasta, Bulgaria	40 ± 20
Whole blood	Athens, Greece	165 ± 33
Whole blood (benign mamma carcinoma patients)	Vienna, Austria	66 ± 21*
Whole blood (malign mamma carcinoma patients)	Vienna, Austria	71 ± 17*

*Sager 1988, unpublished

Table 39: Whole blood Se levels in Europe [SAGER, 2006; modified]

For a better definition of the Se status a recent examination of Austrian people was used. For this purpose, only Austrian determinations could be consulted. Stückler et al. (2008) analyzed the selenium concentrations in the blood plasma of healthy Styrians from 2001 to 2006. The mean selenium concentrations were 93±24µg/l (median: 90; range of 34-341µg/l). At this point it has to be mentioned, that plasma or serum contains about 75% [SAGER, 2006] or rather about 80% of the selenium found in whole blood [SAKR et al., 2007]. Thus, the averaged whole blood values are approximately 124±32µg/l of healthy Styrian people. The selenium level increased curvilinearly with advanced age. It reached its maximum in the age group between 50 and 59 years with about 97µg/l, which complies with about 129.3µg se/l of whole blood. If this is true, the results of the present research showed the subjects'

maximum blood Se values. This showed that the present test persons had definitively lower limits. In the previous determination of 1992, selenium concentrations in blood plasma of Styrian people were about 67µg/l, which complies with about 89.3µg se/l of whole blood [TIRAN et al., 1992]. Nevertheless, it was higher than that of the present study. Again, it was found, that sex had no influence on the blood selenium concentration. The main reason for the positive increase of selenium levels is the supplementation of animal feeds [STÜCKLER et al., 2008]. The blood values in Stückler's study were generally much higher than those of the present subjects because his test persons were healthy. It clarified the difference between healthy and – as in this study – people with thyroid diseases.

The whole blood selenium level was 104.1µg/l in male and 103.6µg/l in female patients. With it, it is shown that there is no difference in the Se level between the sexes. In contrast to that, Oster (1992) noted that the whole blood selenium content clearly shows gender-specific differences. Men have a slightly higher plasma selenium concentration in the intravascular room than women. The Se status of women stronger seems to underlie biological variations, for example, menstrual selenium losses [OSTER, 1992]. Perhaps the recent result is due to the low amount of men among the subjects. It is also possible that thyroid patients have a general diminished blood Se concentration, where a gender-specific difference cannot be seen. The lacking of difference in gender accords with Levander et al. (1984) too. They found that men - although they consume more selenium in diets than women - had similar plasma selenium levels to women. Thus, Levander's result accords with the recent research. Also the more actual finding by Swanson et al. (2008) is in line with it. It was demonstrated that men and women have similar mean values of whole blood despite higher selenium intakes in men [SWANSON et al., 2008]. Again, this also affirms the actual study's outcome. Consequently, it is more or less proved that there is no difference between men and women in their blood selenium levels.

The different reference values showed that it is definitively very difficult to define if there is any deficit or if there is not. But generally, a decreased blood Se level could be manifested.

Despite of the disagreements of scientists, it can be said that recommendations increased in the process of time. Maybe they were adapted to the higher intakes because of the supplementations of animal feeds. It is not surprising that *biosyn*,

which produces selenium supplements, advises higher ranges of blood Se levels. Nevertheless, it really seems that the upper limit of normal blood Se range has to be around 160µg/l. For comparison, Winnefeld et al. (1995) even showed an upper limit up to 168µg/l. Furthermore, according to Sager (2006), the mean Se values in serum or blood vary from 55-185µg/l, which depend on local Se levels and on nutritional habits. Here again, the upper limit of 185µg/l by Sager is much higher than the recommendation of biosyn (2009).

For a definition of a real lowered Se level in total blood further values were used. For the diagnosis of a selenium deficit the scheme below may be helpful.

Serum/Plasma (µg/l)	**Whole blood (µg/l)**	**Erythrocytes (µg/g Hb)**	**Result**
Normal >50	Normal >60	Normal >0.2	Inconspicuous
Low <50	Normal to low	Normal to low	Medium-term undersupply
Low <50	Low <60	Low <0.2	Long-term undersupply
Normal >50	Low <60	Low <0.2	Undersupply in compensation

Table 40: Diagnosis of Se deficit [Selen in der Umweltmedizin, 2006; modified]

According to Table 40, a long-term undersupply occurs when whole blood Se levels are lower than 60µg/l. When regarding the recent study's result, there does not seem to be a Se deficit. As the subjects' lower range of their blood Se level is 68.9µg/l, there is no (heavy) deficiency.
Generally, the height of the total blood selenium level is crucial for the existence or the development of a disease. So, the comparison within the subjects' individual selenium values was more important. Particularly, a general comparison of the Se level of thyroid patients and healthy test persons was made.

Blood selenium level was 103.7±15.6µg/l and 106.7±12.2µg/l in patients with and without autoimmune disease respectively. Both are in the normal range. A slightly lower limit could be seen in people with autoimmune thyroid diseases. It is 88.1µg/l in people with autoimmune disease and 94.5µg/l in healthy people. But the upper range is almost similar. Again, this analysis showed that there is a difference in the

selenium status of healthy subjects and people with autoimmune diseases of the thyroid. Nevertheless, it is normal according to Table 40.

Even if some subjects have a slightly decreased blood Se level, it is not very critical because the amount in the various tissues can be used when the need arises [OSTER, 1992]. Furthermore, a decrease of the plasma selenium content is not necessarily associated with the loss of the antioxidant function. Selenoproteins particularly can be acute phase reactants [STREHL, 2006].

5.2.2.2. Selenium level and thyroid states

A very meaningful result is that the mean blood selenium level was significantly different comparing patients with various thyroid states. It was 94.8±13.4µg/l in patients with hypothyroidism, increasing to 103.2±17.4µg/l in hyperthyroid and further increasing to 108.4±15.9µg/l in euthyroid subjects.

Figure 16 presents very well the high blood selenium level of euthyroid people in contrast to hypo- and hyperthyroid subjects.

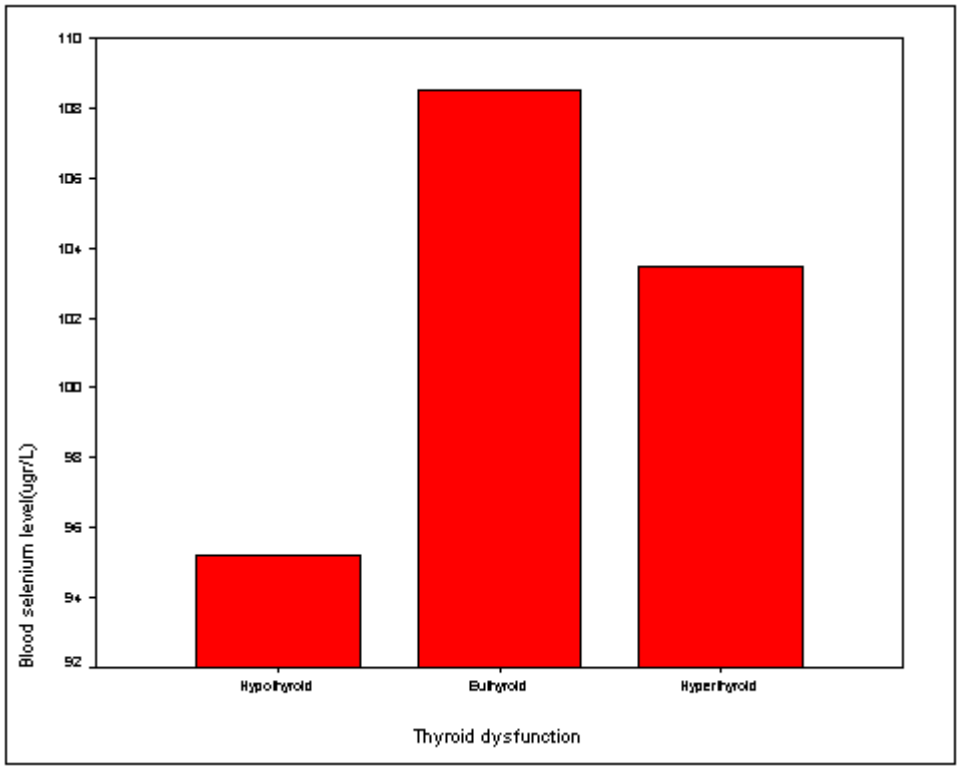


Figure 16: Selenium levels in different thyroid states

The blood selenium level of the present euthyroid subjects ranged from 92.5-124.3µg/l, which is in the optimal range by Winnefeld et al. (1995: 89-168µg/l). Furthermore, it is in the upper range of the reference values by the *Umweltbundesamt* (2002: 79-130 by men, 60-120µg/l by women) and it is somewhat lower than the recommendations by biosyn (2008: 100-140µg/l; 2009: 120-160µg/l). Generally, it can be assumed that euthyroid people do not have a decreased Se level in blood.

Interestingly, there was no significant difference in the blood selenium level of euthyroid and hyperthyroid patients. Rieger (2009), for instance, explained the lowered blood Se levels of hyperthyroid patients as a too high need. This also proved the recent finding. Inversely, it is a fact that the selenium level was significantly higher in euthyroid compared to hypothyroid subjects. Hypothyroid patients have the lowest blood selenium concentrations of the subjects. Maybe because of the lower production of thyroid hormones and consequently, the decreased need for the trace elements. As already well-known - selenium is a particularly important factor in the conversion of T_4 to T_3 and if this trace element is not available thyroid hormones cannot be produced in an adequate amount. Reversely, a Se deficit seems to cause hypothyroidism because without selenium thyroid hormones cannot be activated. Furthermore, the antioxidative defense does not work either. It would be very interesting if there is a lowered blood selenium level first, which causes a disease, or if the disease causes the diminished Se level in blood.

Benamer et al. (2006) also found that people with hyper- and hypothyroidism had significantly lower blood Se concentrations than healthy people [BENAMER et al., 2006]. Again, this validated that healthy thyroid subjects had a higher blood selenium content than people with thyroid dysfunctions.
Summing up, the research demonstrated that blood Se levels are higher in healthy people than in people with any kind of thyroid diseases.

The immune mediated thyroid diseases were also compared with the blood Se content. The blood selenium level was 104.9±16.0µg/l in patients with Hashimoto Thyroiditis and 99.4±16.5µg/l in patients with Morbus Basedow. For comparison, Heufelder (2006) found that about 60% of people with autoimmune mediated diseases of the thyroid show a total blood Se level of lower than 55µg/l. But this was much lower than that of the recent study. In contrast to that, people with no

autoimmune disease had a selenium level of 106.7±12.1µg/l. Thus, no significant result could be shown. This may have been caused by the unequal distribution of the special kinds of thyroid dysfunctions among the study population. In 2002, Kucharzewski et al. found that the lowest mean selenium levels were achieved in the whole blood of women with Graves' disease. The highest levels were found in healthy people [KUCHARZEWSKI et al., 2002], as the present study also attested.

5.2.2.3. Correlation between blood Se level and Se intake

A new finding is the significant correlation between the blood selenium level and the TSIS. The revealed coherence between the selenium intake of each subject and the blood selenium concentration even was very high. It is a very interesting result and it is biologically plausible as well.

Particularly when the subjects' selenium intakes totally vary, the blood selenium status is an ideal marker. The used selenium contents of foods of recent Austrian studies showed that the determined selenium values were fairly good. The specificity is sufficient, at least to rank the subjects concerning the selenium intake or dividing them into groups (high vs. low intake).

The comparison of whether the blood selenium level depends on the daily selenium intake is a very interesting point. Thus, a diagram was made. The correlation between the blood Se level and the daily dietary intake of the trace element selenium demonstrates Figure 17.

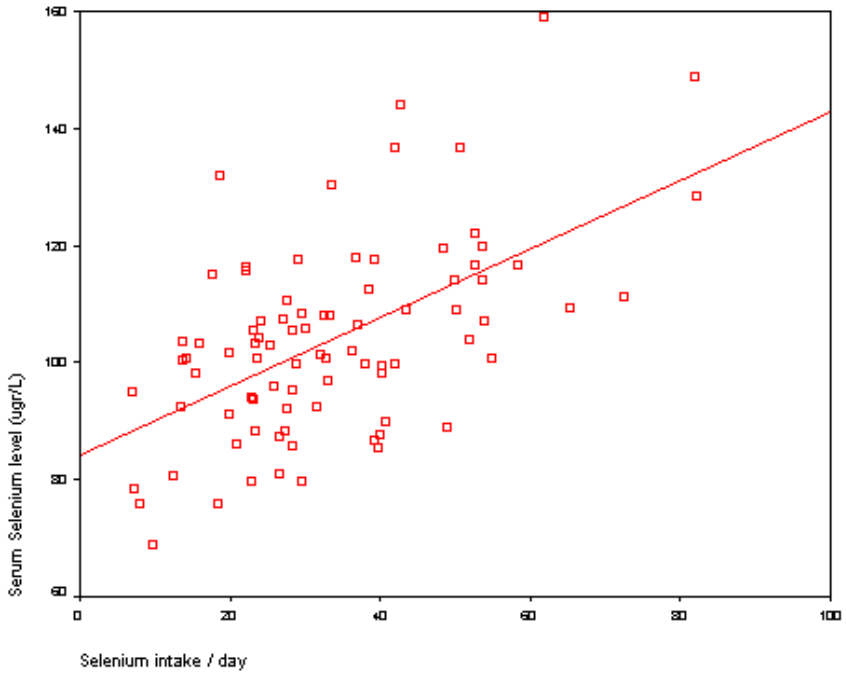


Figure 17: Correlation between the Se level and intake

The correlation between the selenium concentration in blood and the Se intake through foods is clearly indicated in Figure 17. Continually, an analysis was made about the correlation between the blood Se level and the daily Se intake per kilogram of body weight in order to a further more exact investigation.

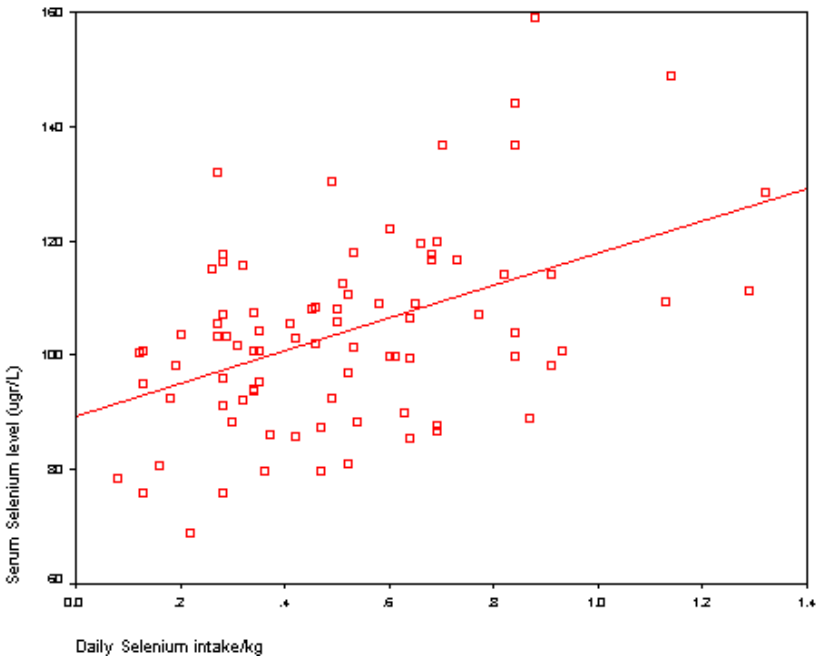


Figure 18: Selenium level and the daily Se intake/kg bw

The selenium intake per kg of bw presents a much better result. Assuming that the calculation of the selenium intake cannot be totally exact, the relations to each other are crucial and seem to be useful.

There have only been very few studies about the link between the Se intake and the blood level up to now. In comparison with literature, only among the Chinese a high correlation between the diet and the whole blood selenium status could be found. It is probably due to the greater range of the selenium intake of that population. In contrast to that, the finding by Longnecker et al. (1991) showed no statistically significant association between the Se concentration and diet [LONGNECKER et al., 1991].

The calculated high significance seemed to show the effectiveness of the self-developed FFQ and its ability to measure the subjects' selenium intake. Even if the Se intake cannot be analyzed exactly, the height of the Se intake and the blood Se level were in right proportion to each other. The result most likely was no coincidence. Therefore, the correlation was too high and clear. The combination of the FFQ with the whole blood selenium determination seemed to interact very well.

5.2.2.4. Thyroid hormones and blood selenium level

Studies also tried to find a correlation between the thyroid hormone values and the Se level in blood. No correlations between fT_3 or rather fT_4 and the blood selenium level could be found, however. Contrary, it was found that the serum TSH level was inversely correlated to the whole blood selenium level. This showed that an augmented TSH level largely appearing in hypothyroidism, leads to a decrease of the selenium level. This could also be affirmed by the analysis of the selenium status of different thyroid states. Particularly, it could be seen that hypothyroid patients have the lowest Se content in whole blood. Maybe - as already mentioned - this happens because of the concurrently lowered thyroid hormone status (T_3 and T_4).

A further point was the surgery. No significant differences in the selenium level between patients who already had and who did not have any thyroid surgery were found. In particular, it was assumed that people who had not had a thyroid operation yet have a lower blood Se level. Through such surgery, thyroid is often removed. But it was not asked in detail.

5.2.2.5. Blood Se level and nodules

The correlation between the blood selenium level and nodules was also examined. Interestingly, patients with hot nodules had significantly lower blood selenium levels than patients with cold nodules. Perhaps hot nodules, which produce a lot of thyroid hormones, use too much of the absorbed selenium. So, the blood Se level sinks. This was true for the Selenium Intake Score per kg of body weight too. The SIS per kg of body weight namely was 0.53±0.25 in patients with cold nodule, 0.44±0.22 in patients with warm nodule and 0.37±0.13 in patients with hot nodule. This showed that people with hot nodules had the lowest Se intake among the three groups. The Se intake reflects its concentration in blood too. Summing up, nodules seem to influence the blood selenium level but there is a need for more detailed research in this field.
Generally, a lot of studies about the essentiality of selenium in goiters were made. Giray et al. (2003) found a link between the trace element selenium and goiter development [GIRAY et al., 2009]. Keshteli et al. (2009) also found that the prevalence of Se deficiency was significantly higher with goitrous than with nongoitrous children [KESHTELI et al., 2009]. These studies also affirmed the correlation between goiter and the blood Se level.

According to the newest results, a selenium deficit definitively prevails among thyroid patients. Generally, nutrition-dependent selenium deficit may appear with protein-poor nutrition and a high degree of regional self-supply because of the selenium-poor Austrian soils. But that can be counteracted, which will be explained in the further analysis or rather in the following chapters.

5.2.2.6. Selenium deficit symptoms

A very interesting new finding is the link between selenium deficit symptoms and the blood selenium level. Generally, individuals are able to adapt themselves to very different selenium supply situations without any deficit symptoms [SIMONOVA and PFANNHAUSER, 2008]. Nevertheless, symptoms can appear.

The number of selenium deficiency symptoms was significantly and negatively correlated with the blood selenium level. This confirms that the worked-out scoring system is fairly good and usable. The more symptoms from the list of main malfunctions were named, the lower was the subject’s blood Se level. The most

frequent symptoms of Se deficiency are presented in Table 41. They were summarized from literature.

Selenium Deficit Symptoms
Myopathies
Fingernails changes (white marks)
Thinner and dull hair
Unintended weight loss
Constipation
Depression
Excitability
Concentration disorders
Low immunity

Table 41: Selenium deficit symptoms

This self-created symptoms list may be used effectively for screening in the hospitals. If there is a suspicion of selenium deficit and a disease respectively, first Se deficiency symptoms can be asked from this list before an expensive blood test has to be done. Of course, this has to be investigated in a better and more thorough way. But this would be a possible approach.

Douptlessly, the mentioned symptoms are indications that often may appear in different diseases, but nevertheless, the result was quite clear.

5.3. Nutrition and thyroid function

Right nutrition plays an important role for an adequate selenium supply. The whole blood Se level is particularly affected by the Se content of foods [OSTER, 1992]. Generally, it has to be born in mind that the bioavailability of selenium in foods is also an important factor [STOJANOVIC, 2000] but of course this could not be evaluated. It cannot be exactly specified either. Approximately 80% of the dietary Se is absorbed depending on the type of consumed foods [NAVARRO-ALARCON and CABRERA-VIQUE, 2008]. So, the selenium contents of the consumed foods were the only possible opportunity for the calculation of the Se intake.

Some studies already demonstrated the link between nutrition and the thyroid function. In 2003, Rükgauer attested that a better nutrition status provides an

increased selenium level in geriatric patients. Doupis et al. (2009) also showed that nutritional factors are involved in the development of goiter in Southwestern Albania. It was particularly striking that all consumed foods were home-produced. But there could not be found any role of selenium [DOUPIS et al., 2009].

Generally, it can be said that individual dietary patterns influence the development of diseases. Thus, it was also determined to see to what extent it influences the thyroid gland. Therefore, the most interesting point of this research was the nutrition habits of the thyroid patients.

5.3.1. Nutritional habits of the subjects

5.3.1.1. General dietary patterns

There were only two vegetarians among the 212 subjects. Thus, the remaining test persons ate meat and other foods of animal origin. This would lead to the assumption that meat may influence the thyroid function negatively. But as a large part of humans eat meat in general, it is highly likely that it is a coincidence. Apart from that, no other nutritional forms, like macrobiotic diets or the nutrition concerning the Traditional Chinese Medicine (TCM) were mentioned. Maybe this is an indication for the not very high significance of the subjects' daily nutrition in comparison to people who eat on the basis of special dietary forms. Only when people adhere to a particular diet, they take their nutrition seriously. But for more detailed information, thyroid patients with special dietary forms have to be studied in more intensive ways in order to be able to draw conclusions.

The selenium concentration in food depends - as already known - on its protein content. So it was asked which main nutrient accounts for the major part of an averaged meal. The main nutrients are proteins and carbohydrates, but it was also asked if the nutrition is balanced. Yet, no differences in the blood Se level of people who thought to eat a more protein-rich or carbohydrate-rich nutrition, or a balanced diet could be found. The result may be explained by people's common ignorance of the nutrient contents and composition of food. As questions were only asked according to self-assessment, the result was not satisfying. It was particularly expected that people who eat a protein-rich diet have a higher blood Se level. A protein-rich nutrition augments the availability of selenium. In Germany, for instance,

the daily selenium ingestion mainly occurs through animal proteins, which accounts for about 65% to the total selenium ingestion [WISCHNEWSKI, 2005].

One aim of the interviews was to find whether a change in diet also affects the health status of a thyroid patient or rather in how far it influences the thyroid function. But in relation to such modifications no changes of the TSH level could be found, comparing values of Laboratory I and Laboratory II. That is true for hypothyroid, hyperthyroid and euthyroid patients. So, nutrition alone does not seem to influence the TSH value. It is a very crucial fact, however, how long a person has changed his/her nutrition. As all the test persons had a change within a year, it is clear that there cannot be a drastic impact. At this point, also more research is necessary.

The appearance of thyroid diseases did not depend on the dominant consumption of regional products. The blood Se level also did not show any correlations to the non/ consumption of regional products. The mean blood Se level particularly was 105.5±16.6µg/l compared to 102.6±16.7µg/l in patients with and without the main consumption of regional products. Although it was expected that people who mainly eat regional products have a decreased blood Se level, the result showed no big difference. Imported foods namely, have largely higher selenium concentrations. This was confirmed by the Bundesinstitut für Risikobewertung in 2004. There it was noted that imported foods generally raise the Se levels of Europeans. A possible reason for this unexpected result was that consumers often do not know where their consumed foods really derive from. Furthermore, some people are not even interested whether the food they buy are grown or produced in Austria or whether it comes from abroad. For such reasons, this question did not gain the expected result.
The origin or rather the quality of food plays an important factor. Stückler et al. (2010) found that meat samples with the *AMA-Seal of Quality* showed the highest selenium contents with about 96µg/kg, followed by meat of biological and conventional production. This demonstrated that food quality also plays an important role for the Se content in food.

Selected selenium-rich foods were summarized into food groups. Then, they were analyzed regarding their contribution to the selenium absorption. Figure 19 shows the contribution of single food groups to selenium ingestion.

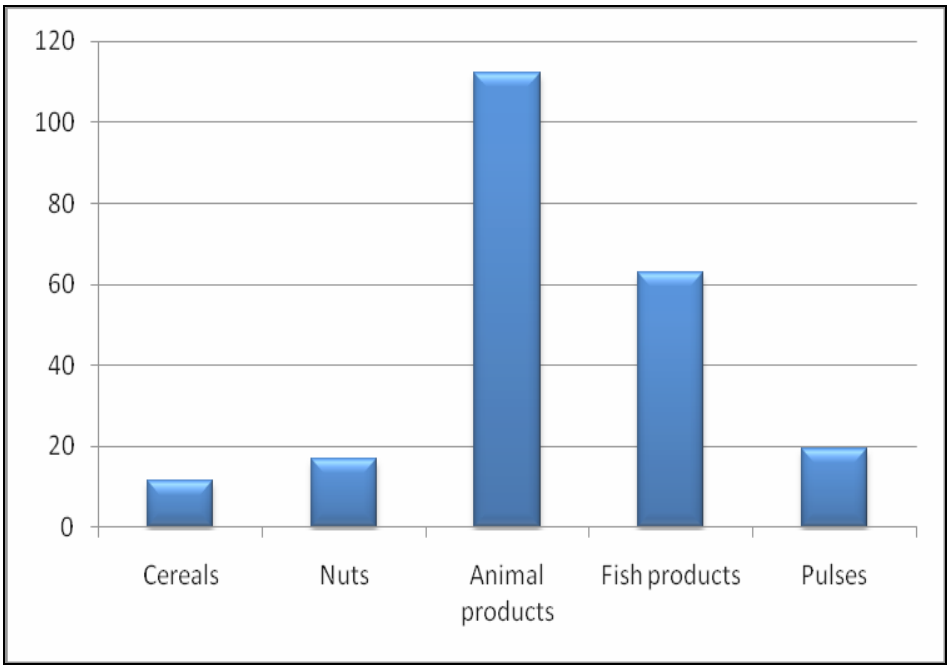


Figure 19: Selenium Intake Score (SIS) of the food groups

Animal products are definitively the main Se suppliers for the Austrian population, followed by fish and seafood. But without the enrichment of animal feeds the Se contents of animal products would be very low. This is also affirmed by the study by Oelschläger and Menke (1968). Pulses, nuts and cereals contribute only to a (very) small part to the Se supply of an organism, probably depending on the consumed amounts.

It can be noted that meat, milk, and eggs provide about more than 100µg and fish around 60µg selenium per week. In contrast to that, pulses, nuts and cereals only add less than 20µg selenium to the dietary selenium intake. These results agree with the determination of German foods by Oster, conducted about 1992.

As a matter of interest and for making better comparisons, analyzes with German selenium contents of foods were made in order to see if there is really a difference to Austrian selenium contents and to which extent. This was made with the food list by Nutri-Science GmbH, PRODI 5.6 (Souci Fachmann Kraut, SFK), which includes averaged values of the selenium concentration of different German foods. There could not be found any definite correlations between selenium intake and blood selenium level. As expected, there is a big difference to the calculation of Austrian foods' selenium contents. It is a proof of the varying soil Se contents. Nevertheless, the difference between the Se concentrations in soils and consequently in foods consists between countries.

As evidence to the contrary, the selenium-poorest foods from the FFQ list were excluded from the analysis to see the effect on the blood Se level. So, the food groups of cereals and pulses, but also of freshwater fish were excluded to make a reverse examination. The new analysis showed that the correlation coefficient was slightly lower. Nonetheless, both were statistically significant. Deleting these foods with the lowest Se content (in contrast to the others) from the analysis did not have a significant effect on the correlation. It even lowers it minimally. This shows that even the consumed amounts do not play an important role for the selenium intake when the foods' selenium contents are low generally.

Thus, se-poor foods do not substantially contribute to the Se intake. Nevertheless, the consumed amount does not seem to be an important factor. But this has also to be studied more extensively.

5.3.1.2. Foods and their contribution to the Se intake

All patients ate bread. So, no comparisons between bread-eating and non bread-eating subjects could be made. It needed to be tested namely to what extent bread consumption contributes to the selenium intake.

Interestingly, the consumption of whole-grain bread did not show any differences in the blood Se level to people who almost entirely consume wheat bread. It was thought that the main consumption of whole-grain bread is reflected in a higher blood Se concentration of the subjects. Maybe the proportion of whole-grain pastries is too low in the daily nutrition or the subjects' answers were not correct. Most people think they eat wholemeal products but the ingredient lists often say the opposite. Very frequently, bread consists of a low amount of whole-grain flour mixed with wheat flour. The bread's color often deceives the consumers. It has to be born in mind that people commonly either eat bread or muesli in the morning. The general consumption of muesli did not show higher blood selenium values of the test persons either. It could not exactly be determined either which type of muesli people ate. Muesli that consists mainly of natural wholemeal flakes naturally provides more selenium and other essential nutrients than industrially produced cereals like cornflakes or chocolate-containing flakes with added sugar.

Thyroid disease was seen in 86% of patients with and in 94.8% of patients without cereal consumption. Thus, it could be supposed that cereals may influence the thyroid positively. The nutrients included in cereals seem to have positive effects on

the organism or rather on the thyroid gland. The B vitamins contained in cereals, for instance, are very important for the thyroid metabolism.

According to the present research, the regular consumption of nuts and pulses, which rather refers to their weekly consumption, did not significantly increase the selenium level in blood. This result was not expected because paranuts have such a high Se content. But there was found that the subjects most frequently consumed peanuts and walnuts. Consequently, there was pointed out that paranuts are not eaten very often in Austria. As of the low offering of paranuts on the Austrian market, they do not (or rather cannot) contribute largely to big parts to the selenium supply. Paranuts namely only are to be found in small quantities in assortments of nuts and raisins, in so-called “student food”.
The amino acid tyrosine – as already known – is part of the thyroid hormones. Although nuts and pulses additionally are rich in tyrosine, their consumption did not show any links to thyroid health [RIEGER, 2009].

The weekly consumption of one to two eggs did not have any effects on the blood Se level or rather the thyroid function. Although eggs contain high amounts of selenium – due to the enriched animal feeds - no significant effect on the Se status could be seen. This shows that eggs must be eaten more often than 1-2 times per week to achieve a crucial effect on the blood selenium level. But people often do not know the exact amount of consumed eggs because of the different ingredients of foods. Apart from that, it is also possible that people did not tell the truth. They know that only a moderate consumption of eggs is advised because of the cholesterol, which is a very controversial subject.

The consumption of milk was considered too. Nearly all subjects drank milk. Only two of the total 212 subjects did not consume any. This was not surprising because Austria is a country with a very big dairy market. Interestingly, the daily consumption of milk increased the subjects’ selenium levels in blood. This is an indicator that the selenium contained in milk can be metabolized by the organism. Additionally, milk contains high amounts of iodine, which probably causes the rise of the blood selenium level too. Generally, it can be said that foods that contain both iodine and selenium influence the selenium absorption positively.

Both, the consumption frequency and the amount of the consumed milk did not show any correlations to the thyroid dysfunction. There was no difference between hypo-, hyperthyroid and euthyroid people either. Thus, milk did not seem to show any negative effects on the thyroid function of the test persons. This was tested because milk contains a lot of hormones, like sexual and growth hormones and such hormones that influence the hypothalamus, the thyroid and the parathyroids [ROLLINGER, 2010]. So, milk only seems to affect the human blood selenium level.

It has to be born in mind that milk is largely consumed with the daily coffee. Maybe the determining factor is that the mixture of coffee and milk enhances the blood Se level because of the antioxidants. Thus, it is advised to drink milk daily. Lactose intolerant people, for instance, are exempt, of course.

The correlation between meat consumption and thyroid function was examined in this study too. Meat covers its mostly eaten kinds, like pork, beef, veal and poultry. Figure 20 shows the consumption frequency of meat in people with different thyroid states.

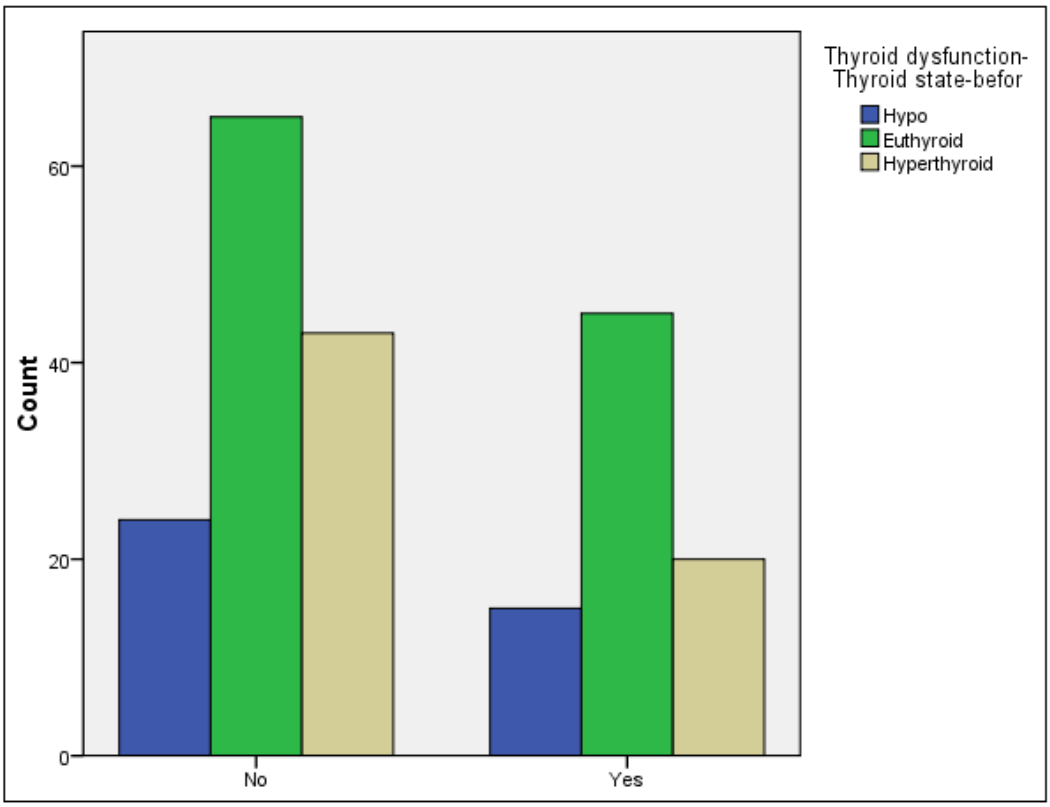


Figure 20: Selenium intake of meat in all thyroid states

For an explanation of Figure 20: For the categorization of the meat consumption, about four times a week or more was summarized as “yes” and less than four times a week as “no”. The y-axis is the number of patients. But there was no significant difference in two groups regarding hyperthyroidism, euthyroidism and hypothyroidism.

The frequency of meat consumption is also of big interest for the Se absorption. The finding was very interesting. The consumption frequency of meat and its effect on the selenium level in whole blood shows Figure 21.

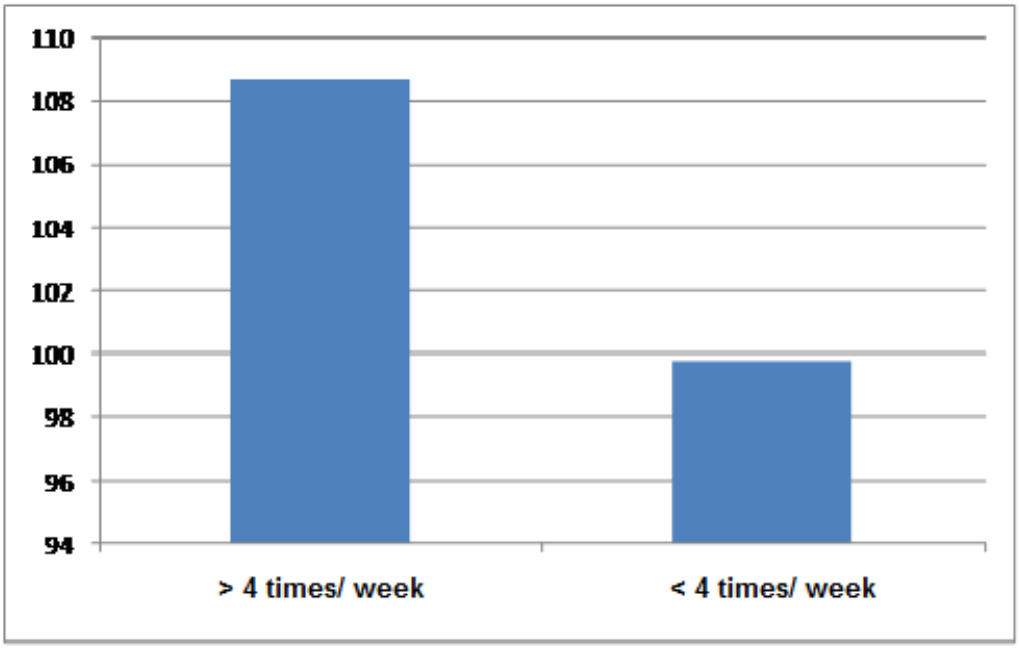


Figure 21: Blood Se level and the frequency of meat consumption

Figure 21 demonstrates convincingly that the meat consumption of more than four times a week is associated with a higher blood selenium level. This shows that animal feeds have made meat an important or rather the most important Se source for humans. The result also accords with Stückler et al. (2010) because pork, beef and poultry contribute to more than 80% to the recommended minimal Se supply by D-A-CH. The bioavailability of selenium in meat can be highly estimated because of its organic bond form [STÜCKLER et al., 2010]. Thus, nowadays, Austrian meat can be seen as an important alimentary Se source.

Furthermore, the consumption of meat does not seem to have any negative effects on the thyroid function, as mentioned before. Particularly, poultry and beef consumption did not show any side-effects on the thyroid function. Meat consumption

can be recommended for thyroid patients if they are to absorb all the essential nutrients and especially the trace element selenium.

Offal consumption seems to affect the thyroid function negatively. More than half of the subjects who do not or hardly eat offal were euthyroid. In contrast to that, only 24% of the test persons who eat offal on a monthly basis were euthyroid. Furthermore, offal consumption did not reflect in the blood selenium level. This was not expected because it is known that offal contains high selenium concentrations. Generally, it is advised to consume offal once or twice a month [ÖSTERREICHISCHE KREBSHILFE, 2002]. But according to the result of the present research, it may be better to eat offal even less often. The purines that are contained in large quantities in offal - contrary to meat that comparably contains small purine quantities - get reduced to uric acid through the kidneys. If the person is hyperthyroid, an elevated concentration of uric acid may be caused. So, the risk for inflammations is augmented.
Again, it has to be mentioned that food quality is a very important topic. Food quality depends on the environmental situation and this leads to a bigger risk of diseases as consequence of a low immunity [ACUFF, 2004]. Often there are heavy metal pollutions or other unwanted substances in foods. The Austrian Institute of Nutrition wrote about this problem too. Elmadfa and Burger (1999) found that offal is strongly contaminated by heavy metals. But this was no big problem because offal was not eaten very frequently, as the present study proved. It should be born in mind that heavy metals interact with selenium. Maybe that is why the subjects' offal consumption did not augment the blood selenium level.
But in spite of the heavy metal contents in food, Elmadfa and Burger (1999) do not advise a lowering of the consumption of vegetables, fish or cereals because of its important nutrient-contributing substances [ELMADFA and BURGER, 1999].

Interestingly, the consumption of fruits and vegetables was slightly higher in patients with thyroid disease (78.4%) than in people with a healthy thyroid (71.4%). But the result was not significant. It is not in accordance either with the study by Eichhorn (2010). He found that if the omega-6 absorption is too low, which is to be found in fruits and vegetables, a thyroid dysfunction may be the consequence [EICHHORN, 2010]. Thus, the actual study's result could not be meaningful. According to the Austrian Nutrition Bulletin (2008) namely, the consumption of fruits and vegetables is

generally not very high. Thus, the authenticity of the answers concerning the fruit and vegetable consumption is limited because of “over reporting”.

The following determination presented a better outcome. A significant difference in the blood Se level of subjects who eat fruits and/or vegetables in contrast to those who do not eat them was found. Subjects who neither eat fruits nor vegetables daily had a lower Se level (96.7±12.6µg/l) than people who daily eat both or rather one of them. The blood Se level was 101.7±14.7µg/l in patients who routinely eat fruits, 107.1±19.3µg/l in patients who periodically consume vegetables, and 107.1±17.7µg/l in patients who eat both. This showed that the daily consumption of fruits and vegetables indeed adds to the selenium supply.
It is very difficult to analyze where the foods are from for determining its Se contents. Maybe this result indicated that mainly imported vegetables or rather fruits are eaten in Austria. So, higher selenium concentrations can be absorbed. The result confirmed the suggestion to eat fruits and vegetables daily, especially if there is a low selenium status of people with thyroid dysfunction and other diseases respectively.
Furthermore, the reason for the increased selenium level of people with a daily consumption of fruits and/or vegetables may be the further essential nutrients contained in them, like antioxidants. They can positively influence the bioavailability of selenium and they most likely support the selenium absorption. Particularly foods which are rich in vitamin C, like vegetables and fruits, boost the Se absorption. As an adequate dietary nutrient intake is important for a healthy thyroid, fruits and vegetables have to be eaten daily.

A lot of studies showed that the selenium status can be changed with the intake of special dietary fats. They modulate the post-absorptive usage and spreading of selenium [SCHÄFER, 2003]. Thus, the present study also dealt with the consumption of dietary fatty acids. The number of different types of vegetable oils used in people’s households was asked. But the blood selenium levels did not vary in patients who use one or more vegetable oils. Maybe this question was not suitable for this knowledge. Even if people had different oils at home, it did not mean that they also consume them regularly. It is not surprising that a relation between the blood selenium level and the amount of used vegetable oils could not be established. Generally, the consumption of high quality oils plays an important role in human

health. Thyroid patients have to consume different kinds of oils, mainly from fish and vegetable fats, as often reported in literature too.

5.3.1.3. Drinking habits and physical exercises

The daily drinking amount of thyroid patients was also analyzed. It included tap and mineral water but also fruit juices. It wanted to be tested in how far beverages influence the Se level in whole blood. No correlations to the blood Se level could be found, however. It was particularly expected that a daily high drinking amount would affect the selenium level too. The received result is also in accordance with Elmadfa and Leitzmann (1998) but also with Anke et al. (2002). Both noted that beverages hardly contribute to the selenium supply.

Sports activities of the subjects were determined as well. Regular sports activity was significantly higher in patients with no thyroid disease (about 57%) compared to thyroid patients (about 35%). This showed that exercising is part of wellbeing. Shomon (2004) explained that thyroid diseases can increase the craving for carbohydrates, which may make a person less likely to do exercises.
The determination of physical exercises of people with different thyroid states was interesting too. About 36% of hypothyroid, 27% of hyperthyroid and 45% of euthyroid subjects did sports regularly, which was significant. It is possible that healthy people generally feel better and that is why they are more motivated to do sports. After all, it is a well-known fact that thyroid dysfunctions lead to mood swings. This may explain why people who suffer from thyroid dysfunctions are disinclined to do sports.
The blood Se level concerning the sports activity of thyroid patients was examined too. There was shown a mean blood selenium level of 107.9±13.2µg/l with and 102.2±17.7µg/l in patients without regular physical exercises. This demonstrated that the Se levels were slightly higher in people who do exercises regularly. Rükgauer et al. (2003) worked on this topic too. It was also found that there is a connection between the sports activity and blood Se level. The selenium level of geriatric patients decreased significantly with lower mobility [RÜKGAUER et al., 2003].

Regarding the questionnaire, there was no differentiation between the various kinds of sports activities, like strength and serious sports and the frequency of doing them. Generally, intense exercises increase oxidative stress - like with all athletes - and may raise the requirements for antioxidants. However, there is no evidence that such

exercises result in an increased requirement for selenium [KANTER, 1998 and THOMSON, 2004]. It can be generalized that the subjects did not do sports excessively, only about one to two times a week. This showed that no oxidative stress was caused by their not too excessive exercises. It is comprehensible that physical exercises have positive effects on the thyroid function. Particularly, in stress situations, the body pours out a lot of cortisol. So, the immune system is negatively impacted and in this situation only physical exercises can lower the cortisol level again.

Exercises also have a positive side-effect: Sports activities are very important for losing weight and keeping it at a certain level, especially in cases of hypothyroidism [SHOMON, 2002]. So, it was proved that sports have positive effects on the thyroid and the Se level in whole blood. Thyroid patients should include more exercises in their normal course of life.

5.3.2. Consumption of thyroid-influencing foods

With the actual results of the consumption of cabbage, soy and iodine-rich foods it should be taken into account that the exactly consumed amounts of these foods could not be calculated. The data could only be saved with “no, monthly, weekly and daily”. It is very difficult to detect the correct amounts. This also applied to fish consumption.

5.3.2.1. Iodine-rich foods

About 38%, which correspond to 81 of the total of 212 subjects, ate iodine-rich foods routinely. Among them, there are seafood, fish and algae. Most hypothyroid (approximately 41%) and euthyroid people (43%) generally ate iodine-rich foods. In contrast to that, only about 29% of hyperthyroid patients ate them. But the result was not significant. Thus, hyperthyroid patients ate least seafood, algae, and fish. It is already known that a person who frequently eats iodine-rich foods and consequently, absorbs too much of iodine, is more susceptible to thyroid dysfunctions, which was confirmed by the present finding too.

According to Shomon (2002), both, a heavy iodine deficit and an excess of iodine, can cause hypothyroidism. That is why a moderate consumption of iodine-rich foods is necessary, particularly for thyroid patients. But it has to be kept in mind that in

some cases physicians influenced the results because of their suggestions to eat or avoid iodine-rich foods.

Interestingly, the thyroid volume and the blood selenium level did not show any differences in people who consume foods with high iodine contents or do not eat any. Selenium levels in total blood did not significantly differ between patients with regular fish consumption and those who do not eat fish periodically. Even the weekly consumption of fish did not seem to show any effects on the subjects' selenium level. But other determinations found in literature do not agree with it. Significant differences in the plasma selenium levels between Swedish fish consumers and non fish consumers were found [Bundesinstitut für Risikobewertung, 2004]. Furthermore, in districts of Brazil, where higher amounts of fish and pork are eaten, the whole blood Se level is significantly higher too [SAGER, 2006]. Contrary, the present research did not show it. It seems that fish is not such a big Se source for the Austrian population in comparison to other countries. Maybe the fish consumed by the subjects came mainly from Austria, which means that freshwater fish was preferred. This may explain why no difference in the blood Se level to people who do not eat fish could be found. But as the result was not significant, this has to be precisely investigated again.

But it also has to be kept in mind that the preparation of fish causes selenium losses too. It depends on the method of cooking that is about 36-46% according to Reilly (1996). Generally, heat has a negative effect on the selenium content in foods, depending on the duration and intensity [ELMADFA and LEITZMANN, 1998].

Furthermore, no correlation between the thyroid disease and the regular fish consumption could be found. The following diagram, Figure 22, presents the consumption frequency of fish in hyper-, hypo- and euthyroid subjects.

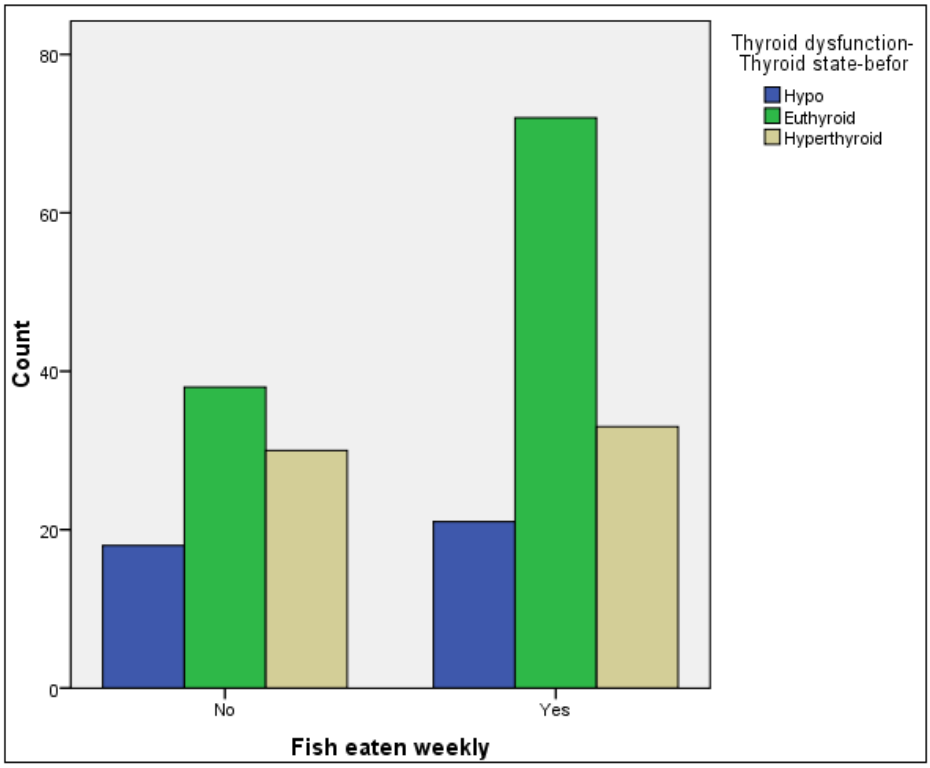


Figure 22: Consumption frequency of fish in all thyroid states

Most subjects who consume fish weekly were euthyroid. Weekly fish consumption seems to influence the thyroid function positively. However, hypothyroid and hyperthyroid patients did not show any significant differences whether fish was eaten weekly or not. As it is known that fish contains - of course depending on its type and origin - both, iodine and selenium, a weekly consumption of fish is advised, especially to thyroid patients.

Interestingly, thyroid disease was more often seen in patients who do not eat shrimps than in those who regularly eat them. The consumption of shrimps seems to have positive effects for thyroid patients. Maybe its iodine content positively affects the gland.

5.3.2.2. Cabbage and its species

Additional thyroid influencing foods are cabbage and other plants of the same species, like cauliflower, broccoli, kohlrabi, Brussels sprouts. The result about the frequency of their consumption was very interesting. Generally, it was much higher in thyroid patients than expected. Ninety percent of thyroid patients ate cabbage products daily or weekly. About 71% of the subjects without thyroid diseases ate them rarely. It is already known that thioglycosides that are contained in members of

the Brassicaceae (Cruciferae) are dietary antithyroid agents [MEANS et. al., 1963 and ASTWOOD et al., 1949]. Generally, glucosinolates produce various by-products, like thiocyanates that are known for their adverse effects on the thyroid metabolism due to competition with iodine [HAN and KWON, 2009]. Thus, ingredients of cabbage species generally inhibit the iodine absorption in the thyroid, as the recent research demonstrated.

Thyroid disease was seen in 92% of patients with a monthly consumption of cabbage, in approximately 92% of patients with daily consumption, and 76% of patients who do not eat it in general. Correspondingly, in a suitable study by Han and Kwon (2009) it was found that the consumption of large amounts of *Brassicaceae* vegetables is correlated with a high incidence of thyroid dysfunction. Truong et al. (2010) found that a high consumption of cruciferous vegetables is associated with thyroid cancer among women with low iodine intake [TRUONG et al., 2010]. The present study proved that a high consumption of cabbage species influences the thyroid function negatively.

			Cabbage intake			Total
			no	Monthly	daily/ weekly	
Thyroid disease	**no thyroid disease**	Count	6	7	8	21
		% within Cabbage intake	24.0%	8.0%	8.2%	10.0%
	Thyroid disease	Count	19	81	90	190
		% within Cabbage intake	76.0%	92.0%	91.8%	90.0%
Total		Count	25	88	98	211
		% within Cabbage intake	100.0 %	100.0%	100.0 %	100.0%

Table 42: Thyroid disease and cabbage

The cross tabulation Table 42 presents very well that a very frequent cabbage consumption of the subjects had a negative effect on the thyroid function.

The mean thyroid volume was 14.3±8.0ml in patients with no cabbage consumption, increasing to 22.9±20.1ml in patients with monthly consumption and further increasing to 24.3±21.7ml in patients with daily or weekly consumption. However, patients with daily or weekly cabbage consumption had larger thyroid volumes

compared to patients who do not eat it. It showed that cabbage vegetables may cause iodine deficit, which makes the thyroid grow excessively.
Means et al. (1963) attested the recent finding. Dietary goitrogenic agents namely are active enough to produce goiter, when they form a major part of the diet. People who eat more than two to three cabbage meals weekly, should pay attention to iodine-rich nutrition too [POLUNIN, 2008]. These results proved exactly that the high cabbage consumption has negative effects on the thyroid.
In order to develop goiter, about 400g white- or 2kg celery cabbage or 2.8kg radishes would have to be eaten for some months, besides an inadequate iodine supply [LEITZMANN and DITTRICH, 2003]. And this is very rarely the case.
People who do not like to reduce their cabbage consumption have to pay attention to the preparation. The cooking process particularly can lower the struma-supporting potential of these vegetables [SHOMON, 2002 and ROMÁN, 2007] and the consumption of iodine-rich foods is also important in this case.

The mean blood selenium level was 102.5±12.2µg/l in patients with a monthly consumption of cabbage, 106.0±20.1µg/l in patients with a daily consumption and 100.0±13.2µg/l in patients with no cabbage consumption. So, cabbage presented positive effects on the blood Se level of thyroid patients. Particularly, cabbage may also contain selenium, depending on its origin [REILLY, 1996]. It was already described that for human nutrition, sufficient selenium can be obtained from garlic, some leafy plants (*brassicaceae*), liver and kidneys. Generally, plants that normally are rich in sulfur, such as members of the *Liliaceae* family, like onions and garlic and the *Cruciferae* family are rich in selenium [SAGER, 2005]. This was confirmed by the result of the present study too.

Thyroid disease was present in 76.0% of patients with iodine food consumption and no cabbage consumption. It increased to approximately 86% in patients with neither iodine nor cabbage consumption and increased further to about 94% in patients who eat cabbage and do not eat iodine-rich foods. This showed that merely the consumption of cabbage causes thyroid diseases, if no iodine-rich foods are eaten at the same time. The present study demonstrated that the ratio between the consumption of iodine-rich foods and cabbage products is very important. When both are eaten in balanced amounts it may not lead to (big) disorders. As cabbage

consumption even elevates the blood Se level of thyroid patients, the consumption of cabbage vegetables and iodine-rich foods (fish and seafood) is advised.

5.3.2.3. Soy and its products

Another thoroughly examined thyroid influencing food is soy and its products, like tofu and tempeh. Generally, soy is popular as a phytooestrogen. Besides the many bioactive soybean components that yield health benefits, greatest attention must be focused on the isoflavones. In large enough amounts soy functions as a hormone and antithyroid agent. Thiocyanates, isoflavones and certain herbal preparations can interfere with micronutrients and influence the thyroid function [TRIGGIANI et al., 2009]**.** These substances typically inhibit TPO, which disturbs proper thyroid function. Soy may adversely affect the thyroid function and interfere with the absorption of synthetic thyroid hormones [MESSINA and REDMOND, 2006]. Thus, an overconsumption of isoflavones is a risk factor for developing thyroid diseases, especially soy powders or soy-based supplements [SHOMON, 2004]. This all makes soy such an important factor of the present study.

To come back to the recent research, the consumption of soy products was seen in patients with thyroid disease to about 39%, which is less frequent than in subjects without any thyroid dysfunctions, which is about 48%. Contrary, thyroid disease was seen in about 88% of patients with soy products consumption and in about 91% of patients who do not eat them. But this result was not significant.

There was a correlation between soy consumption and thyroid disorders. Panda et al. (2009), in an animal trial, found that soy sterols potentially ameliorate hyperthyroidism (and diabetes mellitus) at a moderate concentration. But at higher concentrations it may exert adverse effects [PANDA et al., 2009]. This also coincides with the recent result. Soy namely seemed to have negative effects on the thyroid function depending on its eaten amounts. There is little evidence that in euthyroid and iodine-replete individuals, soy foods, or isoflavones affect the thyroid function adversively. Hypothyroid adults do not need to avoid soy products [MESSINA and REDMOND, 2006].

Thyroid volume was 21.8±21.9ml in patients who generally eat soy products compared to 23.1±18.9ml in patients with no consumption of it. This finding was not significant either.

The consumption of soy products augmented the blood selenium level significantly. The mean selenium level was 109.2±19.7µg/l in patients who eat soy products compared with 100.3±13.2µg/l in patients who do not eat them. In the model of Yan et al. (2010), for instance, Se from naturally produced soybeans is highly bioavailable and they are a good dietary selenium source. This was also verified by the present study.

Summing up, eaten in small amounts, soy has positive effects on the thyroid, since large quantities function as an antithyroid agent. Consequently, soy consumption should be moderate and at the same time iodine intake should also be adequate.

5.3.3. Participants' intake of stimulants

The consumption frequency of alcohol, chocolate, tea and coffee but also smoking habits were determined. Thus, the possible effect of these stimulants on the blood selenium level and on thyroid function was part of this research.

5.3.3.1. Alcohol and especially beer

Alcohol drinking is interesting for this survey because alcoholics are known as risk groups for selenium deficit. The mean Se elimination in urine is reduced in alcoholics too [ELMADFA and LEITZMANN, 1998]. The analyses regarding thyroid diseases and the individual alcohol consumption shows Table 43.

			Alcohol consumption				Total
			no	monthly	weekly	daily	
Thyroid disease	No thyroid disease	Count	8	11	2	0	21
		% within Alcohol consumption	10.3%	11.3%	6.9%	.0%	10.0%
	Thyroid disease	Count	70	86	27	7	190
		% within Alcohol consumption	89.7%	88.7%	93.1%	100.0%	90.0%
Total		Count	78	97	29	7	211
		% within Alcohol consumption	100.0%	100.0%	100.0%	100.0%	100.0%

Table 43: Alcohol drinking habits of thyroid patients

Thyroid disease was seen in about 90% of patients who do not drink alcohol compared to about 11% of the patients who drink alcohol monthly. Thyroid dysfunction was also seen in about 7% of the patients who drink it weekly, and in no subjects who drink alcohol daily. But the result was not significant. So, important conclusion could not be taken.

Euthyroidism was noted in approximately 54%, 59%, and 57% of patients who drink alcohol monthly, weekly, and daily respectively. Contrary to that, 46% of the people who do not drink any alcohol are euthyroid. This result seems to show that the weekly consumption of alcohol has positive effects on the gland's function. But it has to be born in mind that there were many more subjects with euthyroid states among the study population. Apart from that, about 90% of the subjects who do not drink alcohol, suffered from thyroid diseases too. This refutes the assumption that alcohol may have positive effects on the thyroid.

It has to be mentioned that questions about alcohol drinking habits embarrass people and their answers are slightly or totally misleading. Some feel too ashamed to admit the truth, which of course falsifies the results.

Summing up, there was no significant effect from the alcohol consumption on the thyroid gland.

The effect of alcohol on the blood selenium level was also examined. There were slightly higher blood Se levels in people who drink alcohol (105.9±16.0µg/l) in comparison to people who avoid it (100.8±17.3µg/l). But the mean blood selenium level was not significantly different with or without alcohol consumption in general. This showed that alcohol does not affect the Se level either. This finding was not surprising because according to Dutta et al. (2006), the selenium content of various

alcoholic beverages is very low. Furthermore, Korpela et al. (1987) noted that alcohol has even a negative effect on the selenium status because the hepatic structure may be changed by alcohol consumption [KORPELA et al., 1987]. This is an indication for the fact that the consumption of high amounts of alcohol even affects a decrease of the Se level. The study by Dutta et al. (2006) showed significantly lower mean plasma selenium levels in alcoholic subjects than in the controls. People were only asked if they drink alcohol monthly, weekly, daily or not at all. The exact amount could not be found, which made no definite result.
Depending on the consumed amount, alcohol seems to have different effects on the gland. Brakebusch and Heufelder (2007) pointed out that low amounts of alcohol are unproblematic with mild courses of disease. Thyroid inhibitive drugs, like Thyreostatika, can stress the liver too. Thus, alcohol has to be avoided, especially in connection with additional drugs, like beta blockers. This recommendation applies for both, Hashimoto Thyroiditis and Grave's disease patients.

Generally, in the process of thyroid diseases, a lot of patients show alcohol intolerance. Even the liver can be affected by the disease and so the regular reduction of alcohol does not work ordinary any more [BRAKEBUSCH and HEUFELDER, 2007]. Again, this indicated that thyroid patients should better consume alcohol beverages only in moderate quantities or avoid it at all.

The beer consumption of thyroid patients was also determined. According to some sources of literature, beer contains selenium too. Generally, the nutrient supply of beer is composed of dextrin, protein fractions, B-vitamins, trace elements and mineral nutrients, like high amounts of potassium and magnesium [LECHNER, 2010]. The natural antioxidants of malt (barley) and hops in beer have a positive health effect. They may be more readily absorbed than from solid foods. Many studies showed that flavonoids in hops protect against diseases and help fight some types of cancer [WITHERIDGE, 2004]. But in the present study no correlations between disorders of the thyroid and the healthy thyroid of beer drinking test persons could be found. Euthyroidism was noted in about 51% of the beer drinking subjects and in about 52% of no beer drinkers. The analysis of the beer drinking habit is shown in Table 44. For this purpose, the *chi-square test* was performed.

			Beer drinker		
			no	yes	Total
Thyroid dysfunction-	Hypothyroid	Count	22	17	39
Thyroid state-before		% within beer drinker	17.2%	20.2%	18.4%
	Euthyroid	Count	67	43	110
		% within beer drinker	52.3%	51.2%	51.9%
	Hyperthyroid	Count	39	24	63
		% within beer drinker	30.5%	28.6%	29.7%
Total		Count	128	84	212
		% within beer drinker	100.0%	100.0%	100.0%

Table 44: Thyroid dysfunction and beer consumption

No significant differences in the kinds of thyroid dysfunction and beer drinking habits could be found.

Furthermore, no difference in the blood Se levels in patients who drink and do not drink beer respectively were found. This result corresponds with Sager (2005) because among beverages beer hardly contributes to the selenium supply. It was thought that the antioxidants contained in beer have positive effects on the selenium level in total blood.

5.3.3.2. Smoking and thyroid

According to literature, smoking influences the thyroid gland and that is why it was also incorporated into this research.

Smoking was seen in about 63% of patients with and in about 62% of patients without thyroid disease. This obviously did not show any difference.

Particularly, about 64% of hypothyroid, about 62% of hyperthyroid and approximately 62% of euthyroid patients were smokers. So, no significant differences could be noted between the different thyroid states and smoking habits either.

The blood levels of anti-TPO, anti-Tg and TRAK did not differ in smokers and nonsmokers too.

Hyperthyroidism was seen in approximately 23% of smokers, in about 56% of subjects who discontinued smoking, and in about 30% of nonsmokers. This result seems to demonstrate that there is a positive effect of smoking on the thyroid function of hyperthyroid patients. This can be explained by the fact that tobacco smoke is a source of thiocyanates that inhibit the iodine absorption in thyroid [ROMÁN, 2007]. According to that, smoking has a positive effect on hyperthyroid patients. Because of the low amount of subjects with hyperthyroidism, the result in

the recent research was not significant, however. This has to be determined in more detailed studies yet because literature also showed similar results. However, it is better to stop smoking because of many other disadvantages.
According to Vestergaard (2002), smoking significantly increases the risk of developing Grave's disease, including Grave ophthalmopathy but also toxic nodular goiter and Hashimoto Thyroiditis. But the present study could not prove it conclusively.

The mean blood selenium level was not significantly different in smokers compared to patients who do not smoke or stopped smoking. The same was true for the TSIS. This result was not in accordance with literature because smoking increases oxidative stress. So, it augments the requirements for antioxidants like selenium. Maybe the subjects were no addicted smokers, which may have decreased the selenium level significantly. The amount of the usable blood Se data of the smoking subjects might have been too low that conclusive results could be found. Smoking is a cofounder of the decreased selenium content [SWANSON et al., 2008 and SIMONOVA and PFANNHAUSER, 2008].

Czarnywojtek et al. (2001) also proved the negative effects of smoking on the thyroid. It is already known that smoking has negative effects on HT patients because it enforces the deletion process in the thyroid via oxidative damage mechanisms. Therapy-measures are not effective in smokers [BRAKEBUSCH and HEUFELDER, 2007].
Generally, it can be noted that a contamination of heavy metals, like smoking, alcohol consumption and drugs diminish the pool of available se, which is in accordance with Boll and Heinze (2001) and Schünke et al. (1997). Selenium deficit and smoking are among the factors that effectively damage the thyroid [HEUFELDER, 2006]. Even the recent research demonstrated that smoking has to be avoided. Thus, thyroid patients should not smoke.

5.3.3.3. Coffee and Tea

Coffee consumption habits were also examined carefully. Thyroid disease was seen in approximately 11% of patients with a daily consumption of one to two cups of coffee compared to about 7% of patients who drink more than two cups a day. An

interesting finding emerged. Table 45 presents the appearance frequency of thyroid diseases in patients with varying cups of coffee daily.

			Coffee categorized		total
			.00 (≤2cup)	1.00 (>2cup)	
Thyroid dysfunction-Thyroid state-before	Hypothyroid	Count	30	9	39
		% within coffee categorized	20.0%	14.5%	18.4%
	Euthyroid	Count	75	35	110
		% within coffee categorized	50.0%	56.5%	51.9%
	Hyperthyroid	Count	45	18	63
		% within coffee categorized	30.0%	29.0%	29.7%
Total		Count	150	62	212
		% within coffee categorized	100.0%	100.0%	100.0%

Table 45: Thyroid dysfunction and coffee consumption

Coffee does not have any significant effects on the gland's function. Again, the unequal spreading of the thyroid states among the study population can be seen. No significant correlations between coffee enjoyment and thyroid function could be generated. Nevertheless, coffee may have positive effects on the organism because of the simultaneous intake of antioxidants. As already known, antioxidants have positive effects on the thyroid. Lopez-Garcia et al. (2003) found that coffee consumption is inversely associated with markers of inflammation and endothelial dysfunction. This also seems to verify that coffee has a positive effect on inflammation reactions, which can even be applied to thyroid dysfunctions.

Furthermore, the spreading of different thyroid states was not different in patients who drink more than two cups compared to patients who drink fewer. Serum TSH, fT_3 and fT_4 were also not different between patients who drink more than two cups a day compared to patients who drink fewer. This showed that coffee consumption did not influence the thyroid parameters in blood.

A new and significant finding was that the quantity of coffee drunk correlated with the selenium status. As only three subjects drank more than five cups of coffee daily, for a meaningful analysis, these were merged with patients who drink three to five cups

daily. Interestingly, the mean blood selenium level was lower in patients with fewer than two cups of coffee compared to those who drink more daily. Coffee – especially concerning the ingredients contained - has a positive effect on the blood Se level of thyroid patients. Coffee seems to affect thyroid function positively in general.
Generally, it would also have been interesting to know which kind of coffee thyroid patients prefer. There are two main species - *Arabica* and *Robusta* - with different ingredients and amounts regarding their substances. According to a lot of studies *Arabica* is the healthier kind of coffee with, for example, lower caffeine content. But this differentiation could not be made because most people do not know which sort of coffee they generally drink. Thus, this study did not deal with this topic.
Daily coffee consumption is allowed for thyroid patients because it elevates the blood selenium level. Yet, hyperthyroid people should avoid coffee because of its added stimulating effect.

The tea drinking habit was calculated too. The mean blood selenium level was 102.8±16.3µg/l and 108.3±17.3µg/l in patients who drink tea or do not drink tea. Mean TSIS was not significantly different in these patient groups either. It also has to be mentioned that no differentiation was made between the sorts of tea, like black, green or herb. Thus, the results about the tea drinking habits did not show any significant findings concerning thyroid function or the Se status in total blood.

5.3.3.4. Chocolate consumption

Especially in Austria chocolate consumption is very high and so, its consumption frequency of thyroid patients was examined. Chocolate-containing foods were incorporated into this category too. Particularly women consume it. Chocolate consumption was included into the questionnaire to see if it has any effects on the thyroid function. Daily chocolate consumption was seen in about 28% of patients with thyroid disease and in about 33% of patients without any thyroid disorders. This result seemed to show a positive effect on the gland, but it was not significant.

Generally, about hundreds of substances are contained in smallest amounts of chocolate. Lots of nutrients, like iodine or magnesium, and tyrosine, from which thyroid hormones are synthesized, are among the ingredients. But tyrosine is a constituent of nearly all proteins and thus, it can be found in a lot of foods. Tyrosine may therefore not be a significant ingredient of chocolate concerning thyroid function

[HOMORG, 2009]. In contrast to that, the chocolate consumption was also noted in about 33% of patients with hypo- and also in 33% with hyperthyroidism and in about 24% of euthyroid subjects. Thus, the study showed that people who eat chocolate or chocolate-containing foods daily were more often hyper- or hypothyroid. Negative effects between chocolate consumption and the thyroid could even be seen.

But the crucial factor is in which amounts chocolate was eaten daily and which cocoa content was in the consumed chocolate. There are big quantitative differences of ingredients in dark and milk chocolates, which would have to be taken into account as well, if investigated. For organizational reasons more detailed questions could not be asked.

The mean blood selenium level was 104.0±15.9µg/l and 103.9±17.5µg/l in patients with and without daily chocolate consumption. According to this, chocolate did not have any effects on the blood selenium level of humans. It also has to be kept in mind that not all subjects told the truth about their real frequency of chocolate consumption.

The mean TSH and fT_3 status was not different between patients with daily consumption of chocolate and those who do not eat it daily. The mean fT_3 was slightly lower (1.3±0.2pg/ml) in patients with daily chocolate consumption compared to patients who do not eat chocolate or chocolate-containing foods (1.7±1.2pg/ml) daily. Some substances in chocolate seem to inhibit the change from fT_4 to fT_3 slightly but the result was not significant. So, no conclusions could be made.

Maybe chocolate ingredients affect functions of the thyroid. Secondary plant substances, like *flavonoids*, have a variety of biological effects, like antioxidant, or anti-inflammatory activities and regulatory roles on thyroid hormones [RATHEE et al., 2009]. According to Shomon (2004), flavonoids typically act against the thyroid by inhibiting the thyroid peroxidase (TPO), which disturbs the proper thyroid function. Maybe this is the reason why people who eat chocolate daily are more often hyper- or hypothyroid. But in contrast to that, it must also be mentioned that flavonoids are to be found in coffee too. It is well-known that chocolate with a high cocoa amount has a protective antioxidative effect. Furthermore, the chocolate ingredient theobromine, for instance, stimulates the central nervous system. Salsolinol blocks different enzymes, which leads to oxidative stress [HOMBORG, 2009]. Of course,

there could be investigated in how far ingredients of chocolate influence the gland's function.

It has to be mentioned too that some ingredients with negative effects are also contained. According to literature there is a correlation between isolated sugar and diseases. Isolated sugar, e.g., may cause the development of the hyper- or hypothyroid state of the gland because it needs different essential nutrients like vitamin B_1 or calcium, for elimination in the body. So, essential nutrients are additionally used [LEITZMANN and MILLION, 1988]. A further negative influence of sugar is the hyperacidity, which reduces mineral nutrients in the body and creates good conditions for bacteria [ACUFF, 2004]. Perhaps this is why chocolate did not increase the Se level, despite their antioxidant content. Generally, a high intake of isolated sugar, which is largely contained in milk chocolate, shows negative effects on the gland but also other sugar-rich foods have the same negative effect.

There is a big problem with enrichments of heavy metals, especially in dark chocolate. Thus, high cadmium contents may be absorbed with chocolate or cacao, which is very influential in connection with selenium. According to the AGES (2010), for instance, an adult person has exhausted his/her recommendation (TWI-value) to more than 100% by a daily consumption of one bar of chocolate (100g). It has a cadmium content of 0.3mg/kg. That is why dark chocolates should be consumed moderately (max. 30-40g/day). Children should eat half of the amount advised [AGES, 2010]. But besides cadmium, not any other high concentrations of heavy metals in cacao were found [HOMBORG, 2009].
Obviously, the quantity plays an important role. But there is more research to be done in this respect.

According to Acuff (2010), hyperthyroid patients are not allowed to drink coffee and alcohol in general and they also have to avoid sugar. As described above, there are a lot of factors that may have different effects on the thyroid. But generally, only a more specialized analysis would bring more lucidity into this field of research.

5.3.4. Right nutrition for Hashimoto Thyroiditis and Morbus Basedow patients

In particular, when a person suffers from a disease, an adequate intake of nutrients is very important. So, right nutrition by immune thyreopathies, like HT and Morbus Basedow, requires a vitamin- and antioxidative-rich diet [HEUFELDER, 2006 and BRAKEBUSCH and HEUFELDER, 2007]. For thyroid patients also the general recommendations by the ÖGE are effective. Carbohydrates should account for 50-55%, fats for 25-30% and proteins for 15-20% of the daily nutrition. The intake of isolated sugar should be reduced. Dietary fats should be partially substituted for more unsaturated fatty acids because of their anti-inflammatory effects. Apart from that, fruits and vegetables should be eaten daily to augment the intake of antioxidants and other essential nutrients. They even seem to augment the selenium level, as the study showed. Antioxidants are very important because free radicals lead to thyroid damage. Ovaskainen et al. (1993) also confirmed that. He found that dietary β-carotene is a determinant of the selenium status because of their common antioxidant function. Furthermore, nuts should also be eaten. They have anti-inflammatory effects and largely contain mono- and polyunsaturated fatty acids. The ingredients of nuts show a positive impact on inflammatory processes because they lower the peripheral inflammation parameters [DANKERT, 2010]. Thus, nuts like walnuts, paranuts, peanuts, and almonds also have to be part of the daily nutrition. Although it could not be assured absolutely without any doubt that nuts augment the Se status, a tendency could be noted. If, particularly, thyroid patients eat low amounts of nuts, has to be changed. About one to two handfuls daily are advised.

There are only fine distinctions in the appropriate nutrition advice for hypo- and hyperthyroid patients. Hashimoto Thyroiditis patients have to absorb enough omega-3-fatty-acids (fish oils). Hypothyroidism can be caused by both, a heavy iodine deficit and an iodine excess [SHOMON, 2002]. Furthermore, Hashimoto patients should avoid extra iodized foods. However, the natural content of iodine in foods is unproblematic [HEUFELDER and BRAKEBUSCH, 2007]. People with hypofunction should prefer hazelnut oil, proteins from pulses and animal sources, eggs, fish, nuts, especially almonds and hazelnuts but also sesame (seeds) [ACUFF, 2010]. Particularly, in hypothyroidism the glucose metabolism (blood glucose, glucose tolerance test, and insulin level determination) has to be controlled regularly. Generally, HT patients with weight problems have to avoid foods with high glycogenic

index (GI). These foods, particularly, lead to high blood glucose levels and thus, cause high insulin needs. With long-lasting high glucose levels the sensitivity to infections is augmented. Additionally, there is a higher risk for a later diabetes mellitus type II. So, for HT patients it is better to eat five small meals than three big meals daily. In this way, the blood glucose level can be kept constant [HEUFELDER and BRAKEBUSCH, 2007]. Therefore, a frequently used nutrition form by HT patients is the Montignac diet, which is a protein-rich nutrition form. Here, the glycemic index (GI) takes center stage, which often has positive effects on the disturbed carbohydrate metabolism. But the high consumption of saturated fatty acids is disadvantageous [HEUFELDER and BRAKEBUSCH, 2007].
There are also some other therapy forms for hypothyroid patients. The Traditional Chinese Medicine (TCM) shows a very effective method to ease symptoms of hypothyroidism. Alfalfa-sprouts (special corn-type), for instance, act as a stimulant on the thyroid [HU et al., 2010] because of their high content of tyrosine [RIEGER, 2009].

Hyperthyroid patients also have to observe special dietary factors. Patients with Grave's disease are nutritionally depleted in proportion to the duration and severity of their illness. Attention to nutrition is the most important measure. Although the appetite is stimulated, heightened metabolism causes weight loss [MEANS et. al., 1963]. Generally, people with hyperfunction have to avoid iodine-containing foods. Rock-salt is an alternative, till the disorders are getting better. However, in some cases iodized salt can be used nevertheless, because of its low iodine content [BRAKEBUSCH and HEUFELDER, 2007]. B vitamins are very important nutrients for people with a hyperthyroid state of the thyroid. A vitamin B_{12} deficiency often accompanies the autoimmune thyroid disease. It can be made autoimmune by the deletion of the stomach cells, which are involved in the vitamin B_{12} absorption (parietal cells, autoimmune gastritis) [BRAKEBUSCH and HEUFELDER, 2007]. Hyperthyroid people also have a higher demand of vitamin B_2 (Riboflavin). It is contained in green leafy vegetables and in whole-meal products. Natural foods, like balm and hop, also work against hyperfunction. Hyperthyroid patients need absorb too much of the trace element selenium, which may lead to a deficiency [RIEGER, 2009].

The consumed amount of goitrogenic foods has to be considered. In contrast to HT patients, hyperthyroid people may benefit from isothyocyanates and goitrogens because they are natural thyroid arresting substances. Too little of them cause hyperthyroidism and too much can cause goiter [RIEGER, 2009]. The present study has proved this. People, who weekly or daily eat cabbage or its products, more often suffer from thyroid dysfunctions than the others who do not. There should be a balance between the consumption of iodine-rich foods, like sea fish, seafood and algae, and cabbage (-products).
Homeopathy also helps to improve symptoms of hyper- and hypofunction disorders like special *Salts of Dr. Schüssler* [RIEGER, 2009].

5.3.5. Foods for an optimal Se supply

Selenium appears in connection with proteins in animal and herbal foods. Thus, a protein-rich nutrition is very important for thyroid patients. The consumption of whole-grain products is also important, according to Sager and Werteker (2007). In particular, all determined nutrients can largely be found in the external corn layers. Although the present study could not provide a significant result on this particular topic, it is well-known that whole-grain products have a higher nutrient density, which also applies to selenium. So, whole meal cereals have to be preferred to superfine flour products [ACUFF, 2010].
Generally, Austrian pulses and cereals only contain low amounts of selenium. They do not play an important role for the Se intake. However, they contain lots of other essential ingredients. To reach a good protein quality, cereals and pulses should be combined. They complete the intake of important amino acids, which makes them irreplaceable for thyroid patients too.

As the present study showed, the main Se sources are animal products. The reason for the high Se content probably occurs from the supplemented animal feeds. So, pork, poultry and beef are rich in selenium and should be eaten about three to four times a week. Additionally, they supply a wide spectrum of B-vitamins [POLUNIN, 2008], which is mainly needed by hyperthyroid people. Milk also adds to the Se intake, as the study pointed out. Fat-poor milk products but also lean meat should be preferred because they also meet the protein demand. The reduced intake of animal fats is particularly essential. Eggs do not seem to add to the selenium supply but they provide a lot of other essential nutrients all the same.

Fish – besides its high-quality proteins – is a very good source of iodine and selenium. In contrast to literature, the recent analysis could not find any influence of the weekly consumption of fish (freshwater or sea fish) on the blood Se level of Austrian subjects. Fish should be eaten at up to two times a week. But generally, the allowed amount of fish for consumption depends on the kind of thyroid dysfunction. Hyperthyroid people exempt, sea fish has to be part of the weekly menu.

The consumption of nuts did not show any significant result concerning the selenium level. Nevertheless, a slightly higher blood Se level could be seen in people who regularly eat nuts in contrast to those who do not eat them. The same is true for the periodical consumption of pulses. Nuts and beans, lentils and peas, possibly support the selenium absorption in the human organism because of their high protein content.
According to the present study, cabbage products also increase the Se level in blood. But attention must be paid to its antithyroid effects too. The Se level in blood even seems to increase with the consumption frequency of cabbage products. Increasing effects of the blood Se level could also be seem when eating soy products like tofu or tempeh. Furthermore, they can cover the demand of the protein supply as well as animal proteins [Österreichischer Ernährungsbericht, 2008]. Thus, the moderate consumption of soy and cabbage products also seems to augment the blood selenium status of humans.

Even stimulants influence the selenium status of men. The daily consumption of up to five cups of coffee augments the blood Se level significantly. Thus, coffee can be drunk in desired quantities. In contrast to that, chocolate and other sugar-containing foods have to be reduced greatly. Besides oils and dietary fats, the contribution of sweets to the Se intake is negligible [SAGER, 2006]. The alcohol consumption has to be reduced and smoking has to be avoided too.

Generally, a balanced nutrition can compensate the Se deficit. The selenium demand can be met by natural foods. Vegetarians, e.g., can compensate any meat deficit by the consumption of eggs and whole-grain bread [OSTER, 1992]. Paranuts, for instance, are a very important selenium source. According to Thomson (2008) and Kiefer and Haber (2009), one to two paranuts a day even meet the daily selenium requirement. The inclusion of paranuts in the daily diet can avoid the need for supplements to improve the selenium status [THOMSON et al., 2008]. But the resent

research could only prove that paranuts or rather nuts do not play an important role for the averaged Austrian population. Thus, nuts do not rank among the selenium suppliers for Austrians. A further problem is that a lot of people have nut allergies, which rejects the hypothesis to eat paranuts daily in order to meet the Se demand.

For the prevention of apparent Se deficit symptoms a supply of about 0.3µg/kg of body weight and day suffices. This corresponds to about 20µg/d for a 70kg heavy adult [SIMONOVA and PFANNHAUSER, 2008]. Kiefer and Haber (2009), for instance, picked some foods for an adequate Se intake, which meet the daily advised selenium supply.

Kiefer and Haber (2009) made a list with special foods for meeting demand of the daily selenium need. This indicates Table 46.

Amount	Foods
11 g	Pistachios
19 g	Calf-kidney
50 g	Boletus
91 g	Wheat-bread
125 g	Rice
36 g	Herring

Table 46: Foods for meeting demand of the daily Se need [KIEFER and HABER, 2009; modified]

Of course, no general advice for an optimal Se supply can be given because of the varying Se contents in foods. Anyway, it evidences that a well-balanced nutrition can provide enough selenium.

Summing up, three strategies to reach higher selenium levels in the Austrian population have already been developed. First, the employment of se-enriched fertilizers which is not legally allowed to this day and secondly the supplementation of farm animal feeds. The study by Bryszewska et al. (2007), for instance, showed that selenium-enriched rye or wheat sourdough bread elevates the plasma selenium level significantly. Thus, in this way the selenium supply can be augmented too. Attention has to be paid, when too many foods are being enriched with selenium because of its toxic effects. The third method is the consumption of multimicronutrient supplements.

Generally, it it is very difficult to advise taking Se supplements or not. Selenium supplements are mainly beneficial for subjects living in regions with very low environmental Se levels. But because especially in Austria the trend goes towards regional and bio-products, people often cannot absorb enough selenium. This again proves that all things have their benefits and disadvantages. Although usually locally produced foods should be preferred, in the context of selenium, foreign foods should also be eaten. They largely consist of higher Se concentrations.

Supplements have to be advised, particularly, when people suffer from diseases. Also the recent survey proved that people with thyroid diseases have a lower selenium level in blood. Naturally, it depends on the severity of the selenium deficit. The present study verifies that the selenium-rich nutrition plays an important role in thyroid health. In particular, because of its important function in thyroid metabolism. The selenium intake has to be spread over the day because the body cannot store it in high amounts. Although there are individual differences and the discrepancy in the reference values, the adequate Se supply can be defined as 1µg/kg of body weight daily.

According to the ÖGE (2000), people who eat a mixed diet usually do not develop a selenium deficit. However - according to Gärtner et al. (2002) - even mild selenium deficiency may contribute to the development of autoimmune thyroid diseases, selenium deficit must be prevented. Thus, selenium-rich foods generally have to be favored.

5.4. Selenium supplementation considering the case studies

The present study proved that healthy people obviously have higher blood selenium levels than hyper- and hypothyroid patients. Even if it is difficult to define - based on the wide variety of reference values - if there is a Se deficit or not, the comparison to one another subject’s Se level showed the exact distinction. This was also confirmed by Strehl (2006) who noted that ill people have higher selenium needs.
Selenium, particularly, has therapeutic effects on chronic inflammatory conditions [SIMONOVA and PFANNHAUSER, 2008]. The maintenance of adequate selenium nutriture and the selenium deficiency prevention are advisable for all individuals [BOOSALIS, 2008]. A supplementation with selenium may – according to Angstwurm et al. (2007) – prevent a low Se status.

Suitable chemical forms of selenium supplements are inorganic forms, like sodium-selenite and -selenate and organic forms, like selenoamino acids that are selenocysteine and -methionine. Further appropriate forms are more complex organic forms, which occur in se-enriched yeasts and other foods (e.g. wheat and garlic) [SCHÜBL, 2005 and Amtsblatt der Europäischen Union, 2006]. Contrary to Oster (1992), a balanced nutrition alone often cannot compensate a selenium deficit. The body is not able to store it. To achieve a positive health effect the best dosages of selenium are between 100-200µg [BIOSYN, 2008]. The European population absorbs - according to the EFSA - about 27-70µg selenium per day. Thus, the intake of a food supplement that contains 200µg selenium, would augment the total daily intake to about 230-270µg [AGUILAR et al., 2008].

A lot of studies about selenium supplementation and thyroid (dys-) functions have already been made. Hatfield (2001), for instance, could find that selenium supplements protect against diseases in the general population. Gärtner et al. (2002) orally gave female subjects with autoimmune thyroiditis and high a-TPO and/or a-Tg, 200µg sodium-selenite daily for three months. So, the mean TPO-antibody concentration decreased significantly. Selenium substitution improved the inflammatory activity in patients with autoimmune thyroiditis. For comparison, this could also be noticed in the case study I of the present study. Heufelder (2006) also made trials with Se supplementation with thyroiditis patients. He administered them 200µg sodium-selenite for three months. A significant decrease of the TPO-antibodies and a good effect on the general well-being was also shown. It was found that the selenium substitution with thyroid diseases – particularly by immune thyreopathies - is a secure and pathophysiologically meaningful therapy method [HEUFELDER, 2006]. A further study showed that the supplementation of 200µg selenium in form of sodium-selenite-pentahydrat for three months has positive effects of the disease too. But the clinical verification of the selenium effect depends on the kind and amount of the used selenium compounds [STIEFEL, 2009].

In a recent multicentre randomized controlled study by Sakr et al. (2007), 1000µg of sodium selenite were given to 238 critically ill patients (systemic inflammatory response syndrome (SIRS), sepsis, and septic shock) for 15 days. An association with improved survival compared with the placebo treated group could be seen. Serum or plasma selenium levels were well correlated with the erythrocyte GPx

activity by low selenium intakes. With higher intakes, the activity of GPx reaches a plateau [SAKR et al., 2007]. In the study by Angstwurm et al. (2007), it was also documented that the treatment of patients with high-dose sodium-selenite (500-1000µg) reduces the mortality rate of patients in intensive care. It was inversely correlated with the whole blood selenium concentrations. There were no side effects observed due to high-dose sodium-selenite treatment [ANGSTWURM et al., 2007].
This proves that the low selenium quantity of case I possibly has to be heightened because the woman “only” received 150µg selenium daily. Furthermore, Angstwurm et al. (2007) also showed positive effects of a 200µg Se supplementation in patients with rheumatoid arthritis and asthma for three months. It significantly reduced pain and joint involvement [ANGSTWURM et al., 2007].
Besides sodium-selenite, other selenium forms for supplementation are also used. In 2007, Mazokopakis et al. evaluated the effects of selenium supplementation on serum a-TPO levels among Greek patients with HT. AITD patients were treated with 200µg L-selenomethionine per day for three, six, or nine months. There was a significant reduction of a-TPO concentrations. Again, it could be shown that the supplementation modifies the inflammatory and immune responses. Apart from that, it decreases the toxic concentrations of hydrogen peroxide and lipid hydroperoxides resulting from thyroid hormone synthesis [MAZOKOPAKIS et al., 2007]. In 2005, Moncayo and Moncayo showed the influence of the selenium supplementation on the thyroid function too. They administered 200µg of selenomethionine daily and the Se levels returned to normal (i.e. >120µg/l) [MONCAYO and MONCAYO, 2005]. For comparison, selenomethionine was also given to the female patient of case II. Besides sodium-selenite, selenomethionine also seemed to show positive effects on the thyroid gland.

As already mentioned, there are some controversial study results concerning the effects of the selenium supplementation. In an area of Germany and around Athens with marginal dietary iodine and selenium intake, for instance, people were given 200µg selenium. But it showed no effects on the concentration of a-Tg, TSH or thyroid hormones. The mechanism by which selenium exerts effects on a-TPO production is likely to be due to the ability of high doses of selenium to modify the inflammatory and immune responses [BECKETT and ARTHUR, 2005]. Furthermore, in the “Selenium and Vitamin E Cancer Prevention Trial” (SELECT), twenty-eight healthy adults daily took 200µg selenomethionine for 28 months. Here, selenium

supplementation produced no clinically significant change in the thyroid hormone concentration. There only was a small but statistically significant increase in the T_3 concentration noted in humans, with no corresponding decreases in the TSH level. But after 9 months, mean (±SEM) plasma selenium concentrations had increased [COMBS et al., 2009]**.** There has to be added that Combs' subjects were healthy people. Furthermore, there was also only a small study population of twenty-eight people. Nevertheless, Combs' study showed that the duration of the Se supplementation is an important factor, which - besides the particular dosage - has to be studied better. According to the study results already described, the daily Se supplementation of case I with 150µg daily may be too low.

Case study I showed that the selenium supplementation lowered the thyroid antibodies in blood considerably. TPO antibodies even were lowered for more than 50% through treatment with selenium. Although there was a general up- and down-play of the antibodies on the different days of examinations, an obvious decrease of those could be listed. It also has to be mentioned that the woman had a carcinoma, which probably also had changed the immunity of the whole body. Maybe this explains the up- and down-play of the antibody titers. After about 5 months of supplementation, her total blood selenium value increased to 159µg/l. This pointed out the benefits of the selenium donation. Regrettably, the selenium status in the beginning of taking selenium was not measured but it was known that the Se status was much lower in the beginning. According to Merck (2010) – who advises the reference value of 130-160µg/l - the selenium status was obviously within the reference range.

Case study II showed similar results concerning the effects of the selenium donation. The TPO antibodies also decreased due to the selenium intake. However, the dietary selenium supplementation did not change the TSH value. In contrast to case I who took sodium-selenite, this patient received selenomethionine, which also showed a positive effect on the antibody status.

Generally, in various studies, the selenium forms of sodium-selenite and selenomethionine for supplementation were mainly used. Aguilar et al. (2008) noted in the EFSA study that the steady state equilibrium was reached after a 6-12 month dietary supplementation with selenomethionine or selenium-containing yeast. Selenium is built into tissue proteins of the skeletal muscles, the liver, in the

erythrocytes and into plasma-proteins. Afterwards, they can be catabolically liberated. This leads to a big use of selenomethionine, which gets recycled too. The selenium concentration in plasma augments as a reaction to an increase of nutrition caused Se supply. It stays constant a lot of years, if the selenium supply does not change [AGUILAR et al., 2008]. This shows that the Se supply plays a very important role for the selenium status of the human organism.

Another important aspect could be found. The thyroid patient of case study I is a very good example for the possible importance of the intake order of selenium supplements and thyroid drugs. First, the patient took selenium and afterwards Euthyrox, which caused higher TSH values. In contrast to that, when she first took Euthyrox and then selenium, the TSH level decreased. This aspect has to be researched more carefully in further studies to find in how far there is a correlation.

Furthermore, the two case studies emphasize that the height of the antibodies in blood does not necessarily depend on the severity of the disease. If a lot of symptoms are caused by thyroid disorders, it does not in itself indicate that there is a very low blood Se level. But according to biosyn (2010), the lower the selenium blood levels are, the heavier the symptoms. This definitively has to be studied in better ways. However, conclusions can be drawn. It is quite clear, that antibodies in blood are indicators of the development of diseases and selenium definitely helps to milder courses.

Selenium supplementation seemed to reduce inflammations in patients with autoimmune thyroiditis. In HT patients recent clinical studies already documented the suppressive effect of the selenium treatment on the concentration of serum antithyroid peroxidase [MAZOKOPAKIS and CHATZIPAVLIDOU, 2007]. According to the case studies, selenium donation also showed benefits in the initial stage of HT patients. A decrease of the antibodies and a slowdown of the course of disease can be achieved with the donation of selenium. Summing up, it can be noticed that most studies show positive effects of the selenium supplementation. Only few do not show any advancement in the course of disease treatment. Generally, the selenium substitution should be seen as a meaningful and alternative possibility [WISCHNEWSKI, 2005].

Nevertheless, more detailed investigations are needed. Particularly, possible interactions between the Se supplements and other food components and their influence on the Se bioavailability have to be proven.

According to Reilly (1996), the supplementation at the supranutritional level is not necessary to improve immune response. This is why it is important to take Se supplements exclusively under medical supervisions. However, benefits of the Se supplementation are uncertain yet. Indiscriminate use could generate an increased risk of selenium toxicity [NAVARRO-ALARCON and CABRERA-VIQUE, 2008]. The supplementation should be better tested, especially on a long-term basis [BOOSALIS, 2008].

5.5. Strengths and limitations of the study

One main strength of the study is the utilization of the FFQ. It is namely the best method to find the correlation between a special nutrient supply and a disease. Furthermore, the food list was made in a corresponding length because no patient mentioned that the questionnaire was too long or rather stopped it prematurely. Nutrient intakes namely are often overestimated in longer food frequency lists but also underestimated by shorter lists [FREISLING, 2007].

A further main strength is that the FFQ was validated with the use of a biochemical indicator. The blood selenium determination checked the calculation of the Se intake through foods. Thus, the whole blood analysis can particularly be seen as the strength of the study.

The combination of the FFQ with the whole blood Se examination seemed to be successful too. With the FFQ, a longer period of consumption can be evaluated. The whole blood selenium level is a long-term parameter and also responds to the changes in selenium intake [ASTHON et al., 2009].

Besides validation, reliability is also a very important factor of a study concept. The FFQ can generally be used for the calculation of the Se intake of all age stages. The included se-rich foods were not matched on one special population group. The FFQ can also be used for other population groups (in Austria), like cancer patients or people whose selenium intake has to be calculated. Of course, there will be little

variations in asking the same people again about their usual nutritional patterns. But this is unavoidable. In theory, the received results are reproducible.
The high number of subjects is also an asset. This was very important for the authenticity of the results. The attained study population of 212 subjects provided better and more significant findings, although not all blood samples taken could be used. On the contrary, this could also be seen as a limitation. But a lot of studies exist, where a much lower study population was taken, which makes the eighty-nine blood Se data a relatively high number.

The second questionnaire, which included all factors that may influence the thyroid function, was very important for the screening of the thyroid patients too. So, representative conclusions of the individual nutritional habits could be made.

A further strength is that the study could identify the food group that largely contributes to the selenium intake of the Austrian population. Dietary patterns that support or impede thyroid health, could be found too, which is a very important aspect. Even thyroid patients want to know what types of foods are right for them.

At this point, the following also has to be mentioned. For the determination of the selenium intake particularly, no exact data of its food contents are in existence. Nutrient databases do not include the trace element selenium either. This made the examination of the selenium status very difficult. But recent studies helped to work around this problem.

Of course, there are also limitations. The main limitation of the recent study is that the iodine status could not be determined, since selenium and iodine appear and act together in the thyroid. This would make the determination of the subjects' iodine status essential too. With an existing selenium deficit high iodine doses can lead to an impairment of the thyroid for instance [SHOMON, 2002]. An iodine determination could not be made for organizational reasons.

A further limitation is the specification of the consumed food amount and the portion size respectively in the FFQ. People often do not remember or it is difficult for them to define the food amounts eaten. Nevertheless, for accuracy it is important to determine both, the food quantity and its quality.

As the main part of the subjects was middle-aged and older, there is a higher possibility that these patients have to take pharmaceuticals more often. That means, in turn, that the nutrient supply may be affected by it and consequently, the selenium status (despite including the intake of medications in the questionnaire).

A further restriction of this study is that - particularly in older subjects - recall problems of the past diet may appear more often.

The last considerable limitation of the study is that no selenium supplements could be administered to the thyroid patients. Particularly, it was not possible because of the Ethics Commission. The selenium supplementation would have led to significant results. Of course, case studies alone cannot show significant results but they were included as a replacement to it.

5.6. Possible suggestions for improvement

The first and most important suggestion for improvement of the present research is that financial resources have to be available. Only in such a way things can be researched well. Of course, this is not something new, but it is often a problem in any research and it should be mentioned.

Apart from that, more detailed questions could have been to find more about the individual nutritional patterns of thyroid patients. The kind of chocolate (milk or dark) or the type of coffee (Arabica or Robusta), for instance, would be interesting concerning the thyroid function. But this has to be an extra specialized study. In the recent study, it would have claimed much more time and patience of the patients, which was held as marginally short as possible.

More usable blood selenium values would bring more exact conclusions in cases of uncertainties. Thus, much higher blood selenium data are advised for a further study concerning this topic.

More studies concerning Se supplementation and the thyroid gland have to be conducted, however. Particularly, it also has to be evidenced, which form of selenium is most effective, what is the right dosage and for how long Se has to be taken for benefits. Thus, it is advisable to continue this research by giving thyroid patients selenium supplements.

VI) CONCLUSION

The aim of the study at hand was to establish the existence of a correlation between nutritional habits - focused on the trace element selenium - and thyroid function. Therefore, the individual dietary selenium intake and the blood selenium level of thyroid patients were determined. The main findings are presented below.

- ✓ **Total Selenium Intake Score (TSIS)**

No significant differences were found between the mean dietary selenium intake of healthy subjects and patients with autoimmune thyroid diseases. Furthermore, no significant differences were encountered when examining the mean TSIS of euthyroid subjects, hypo- and hyperthyroid patients. The mean concentration of daily absorbed selenium was approximately 33.1±13.5µg among euthyroid subjects, 30.4±12.0µg among hyperthyroid and 30.4±14.5µg among hypothyroid patients. Nevertheless, the mean weekly TSIS seemed to be slightly higher in euthyroid subjects.

Since the EAR is defined with 45µg, the daily Se intake of 86% of the total study population was below average. This indicates that thyroid patients live on a low selenium diet.

- ✓ **Blood selenium level**

Sex, weight and age do not appear to influence the blood selenium level. However, if the balance of the metabolism is upset (e.g. by an inflammation), the blood selenium level seems to drop.

No significant differences were found in the blood selenium levels of patients with and without autoimmune thyroid diseases. However, in subjects without thyroid diseases the values of TSIS and the blood Se levels were slightly higher.

A very crucial and new finding is that the mean blood selenium level significantly differed when comparing patients with different thyroid conditions. The mean blood selenium level was 94.8±13.4µg/l in patients with hypothyroidism, increasing to

103.2±17.4µg/l in hyperthyroid patients and further increasing to 108.4±15.9µg/l in euthyroid patients.
The total blood selenium level of euthyroid subjects was within normal range. This shows that the trace element selenium plays a significant role in thyroid health. In contrast, the blood selenium levels of hypo- and hyperthyroid people were within lower ranges. The blood selenium level of euthyroid subjects was higher, particularly when compared to hypothyroid patients. Interestingly, no significant differences between the blood selenium levels of euthyroid subjects and hyperthyroid patients could be examined. The blood Se level of euthyroid subjects was higher than the blood selenium levels of hyper- or hypothyroid patients.

HT patients seemed to have a slightly higher blood Se level than Basedow patients.

Thyroid volume and the number of thyroid nodules were not related to the blood Se level or TSIS.

Another interesting finding is that patients with a hot nodule had significantly lower blood selenium levels than patients with a cold nodule. This was also true for the Selenium Intake Score per kg body weight.

The most new and intriguing finding is the significant correlation between the whole blood selenium level and the TSIS.

Summing up, the research demonstrated that blood selenium levels are higher in healthy people than in people with any kind of thyroid diseases.

- ✓ **Selenium deficiency symptoms**

The selenium deficiency symptoms were significantly and negatively correlated with the blood selenium level and the TSIS. The number of deficiency symptoms reflected the blood selenium level very well.

- ✓ **Foods containing high levels of selenium**

A considerable result was that the general consumption of the main sorts of meat, like pork, beef and poultry, significantly affected the blood selenium level. Furthermore, meat did not seem to show any negative effects on the thyroid gland.

The mean blood selenium level was significantly higher in patients who consume meat more than four times a week, compared to patients who eat it less frequently.

Another very interesting finding was that the daily consumption of milk increased the blood selenium level. Milk in coffee also was included in this analysis.

The analysis of the consumption of fruits and vegetables - in relation to the blood selenium level – also led to a new finding. Subjects, who eat fruits and/or vegetables daily, in contrast to those who do not, had a significantly higher blood selenium level. Vegetables seem to contain more selenium than fruits. People who eat neither fruits nor vegetables on a daily basis had a much lower Se level than people who eat both several times every day or only one of them.

There is definitively a correlation between the blood selenium level and the human thyroid function. Thus, selenium plays an important role in the thyroid metabolism. As a result, selenium-rich foods should be preferred. The main selenium sources for people who eat a mixed diet are animal foods but also fruits and vegetables.

- ✓ **Foods containing little selenium**

Cereals (including bread), nuts and legumes did not seem to influence the selenium level in blood. The consumption of whole-grain bread did not affect the blood selenium level differently than the consumption of wheat bread.

The consumption of intestines seemed to affect the thyroid function negatively. More than 50% of the subjects who eat offal less than once a month or do not eat offal at all were euthyroid. The consumption of intestines did also not show any changes of the selenium level.

The consumption of one to two eggs per week did not have any effects on the blood Se level or the thyroid function.

- ✓ **Cabbage and soy consumption**

An interesting finding is that thyroid patients consumed significantly more cabbage and other plants of the same species (e.g. cauliflower, broccoli, kohlrabi, Brussels sprouts) than expected. Thus, a weekly or daily consumption of cabbage seemed to increase the risk of suffering from thyroid diseases. Furthermore, high cabbage

consumption seemed to cause larger thyroid volumes compared to patients not consuming cabbage.

Although cabbage seems to add to the selenium intake, cabbage should be eaten in moderate amounts and preferably in combination with iodine-rich foods. Their good balance may prevent thyroid diseases.

The regular consumption of soy and soy products however, did not show any correlations to the thyroid function. It even seemed to elevate the blood selenium level.

- ✓ **Stimulants intake**

Another new meaningful finding was that the consumption of more than two cups of coffee a day increased the blood selenium level. A daily consummation of up to five cups of coffee even seemed to have a positive effect on the thyroid.

Alcohol did not show any significant results concerning the thyroid function, although there was a tendency towards a higher risk for developing thyroid dysfunctions. Alcohol does not seem to have any influences on the blood selenium level as well. The same is true for the beer consumption.

Smoking seems to affect the thyroid negatively, but no significant differences between hypothyroid, euthyroid and hyperthyroid patients could be reported. Even thyroid antibodies did not differ significantly between smokers and nonsmokers. Nevertheless, a slightly positive effect of smoking on hyperthyroidism was reported. The blood Se level was also not influenced by smoking.

Chocolate consumption did not influence the thyroid function significantly, except that the mean fT_3 was significantly lower in patients with daily chocolate consumption compared to patients who do not eat chocolate daily.

A balanced diet with a moderate intake of stimulants influences the thyroid function positively. The exception among the stimulants is coffee, which seemed to have positive effects on the selenium level.

- ✓ **Physical exercise**

It became apparent that physical exercise has obviously positive effects on the thyroid gland. When comparing the habits of healthy individuals with thyroid patients, the number of healthy people exercising regularly was significantly higher compared to the number of thyroid patients.

- ✓ **The study's quintessence**

The findings of the study conducted in the framework of this dissertation strongly suggest that thyroid patients benefit if they live on an adapted selenium-rich diet. The study also proved that selenium plays an essential role for the organism.

VII) SUMMARY

The present study was undertaken to investigate the relation between thyroid abnormalities and the selenium status in whole blood but also to analyze the diet of thyroid patients in general. Subjects were interviewed in the *Wilhelminen*spital and *Kaiserin Elisabeth Hospital* in Vienna from October 2009 to January 2010. Among the 212 subjects there were also 21 people with a healthy thyroid, who were also incorporated in the study for comparisons. The patients' nutritional patterns were recorded through oral interviews.

The FFQ was developed to find the consumption frequencies of selenium-rich foods and the usual portion sizes to define the individual selenium intakes. From five different food groups, a total of 15 selenium-rich foods were selected which are obtainable in Austria. From each food, the selenium content of an averaged portion size was multiplied by the eaten amount and then by the frequency of consumption, in compliance with the key-food method. The second questionnaire set up for this study included personal details, medical information and especially questions about individual nutritional habits. Thyroid parameters, like TSH, fT_3, fT_4 and antibodies, were used for the analysis but also different habits influencing the thyroid, like smoking or coffee consumption, were noted.

For validation of this study, blood selenium levels of 89 subjects were used. After all data were received, they were evaluated with the help of the program software "Statistical Package for Social Science" (SPSS, V 11.5, SPSS Inc.).

Interesting relations between diet habits and thyroid diseases and blood selenium levels respectively, could be found. Indeed, there seemed to be a too low selenium intake among thyroid patients. 86% of the total study population was below the Estimated Average Requirement (EAR). A new and interesting result was that a significant correlation between selenium intake and blood selenium level could be ascertained. A correlation between the selenium content in blood and thyroid dysfunction could also definitely be assessed. The selenium level was higher in euthyroid people compared to hypo- and hyperthyroid patients. Selenium deficiency symptoms were negatively correlated to the blood selenium level and Total Selenium

Intake Score (TSIS). Sports activity had positive effects on the thyroid function. Furthermore, a regular consumption of fruits and vegetables also showed higher blood selenium levels. Animal products, like milk and meat (pork, beef and poultry) played the most important role for the selenium supply.

The study proves that there is a correlation between the selenium level in whole blood and thyroid dysfunction. Parameters, like foods and special habits, were shown to either enhance or decrease thyroid function and/or selenium level. This indicates that nutrition is a very important factor in the development of a thyroid dysfunction or in the amelioration of disease symptoms. Thus, balanced nutrition plays an important role for an adequate selenium intake and for thyroid health in general.

VIII) ZUSAMMENFASSUNG

Die vorliegende Studie beschäftigte sich in erster Linie mit dem Zusammenhang zwischen der Schilddrüsenfunktion und dem Selenstatus in Vollblut. Das Ziel war es, das Ernährungsverhalten von Schilddrüsenpatienten bezüglich der Selenaufnahme über die Nahrung zu analysieren. Die Datenerfassung wurde mittels Interviews durchgeführt. Die Patienten wurden im *Wilhelminenspital* und im *Kaiserin Elisabeth Hospital* (KES) in Wien befragt. Die Erhebung dauerte von Oktober 2009 bis Jänner 2010. Insgesamt wurden 212 Personen befragt, von denen ca. 21 keine Schilddrüsenerkrankung hatten. Diese wurden auch in die Untersuchung aufgenommen, um diverse Vergleiche ziehen zu können.

Um mögliche Rückschlüsse auf die (Fehl-) Funktion der Schilddrüse ziehen zu können, wurde das gesamte Ernährungsverhalten von Schilddrüsenpatienten untersucht. Es wurde ein *Food Frequency Questionnaire* (FFQ) entwickelt, um die tägliche Selenaufnahme der Testpersonen aus verschiedenen Lebensmitteln genau bestimmen zu können. Dafür wurden aus fünf verschiedenen Lebensmittelgruppen insgesamt 15 selenreiche Lebensmittel selektiert („Key Food“-Methode), die es in Österreich zu kaufen gibt und die laut Österreichischem Ernährungsbericht bevorzugt konsumiert werden. Aus dem jeweiligen Nahrungsmittel wurde der Selengehalt pro durchschnittliche Portionsgröße berechnet und sowohl mit der individuellen Portionsgröße als auch mit der Konsumhäufigkeit multipliziert. Auf diese Weise wurde die gesamte Selen-Aufnahmemenge (TSIS) berechnet. Zusätzlich wurde ein Fragebogen entwickelt, der sowohl allgemeine Patientendaten, als auch medizinische Daten und speziell Fragen über die individuelle Ernährung beinhaltete.

Um die Selenaufnahme über die normale Ernährung besser validieren zu können, wurde der Blut-Selen-Gehalt von 89 Studienteilnehmern bestimmt. Schilddrüsenwerte wie TSH, fT_3, fT_4, sowie die Antikörper-Gehalte im Blut, aber auch bestimmte Gewohnheiten, die die Schilddrüse beeinflussen können, wurden ebenfalls ermittelt. Danach wurden diese Daten mit dem statistischen Programm SPSS (SPSS, V 11.5, SPSS Inc.) ausgewertet. Dies führte zu neuen Erkenntnissen auf diesem Gebiet.

Bezüglich der Estimated Average Requirement (EAR), nahmen 86% der Studienpopulation zu wenig Selen täglich zu sich. Es wurde eine signifikante Korrelation zwischen der Selenaufnahme über die Nahrung und der Selenkonzentration im Blut gefunden. Außerdem zeigten die Testpersonen im euthyroiden Zustand höhere Blutselengehalte als Personen mit Über- und Unterfunktion. Studienteilnehmer, die regelmäßig Sport trieben, litten seltener an einer Schilddrüsenerkrankung als Personen, die kaum bzw. keine Bewegung machten. Weiters waren Selenmangel-Symptome mit dem Selen-Blutgehalt und der gesamten Selenaufnahme über die Nahrung negativ korreliert. Der tägliche Konsum von Obst und Gemüse trug zudem auch zu einer besseren Selenversorgung bei.

Es konnte ein Zusammenhang zwischen dem Selengehalt im Blut und einer Schilddrüsenfehlfunktion beobachtet werden. Bestimmte Parameter, wie Lebensmittel und (Ernährungs-) Gewohnheiten, konnten aufgezeigt werden, die die Schilddrüsenfunktion entweder verbessern oder hemmen. Essgewohnheiten spielen daher auch bei Schilddrüsenerkrankungen eine große Rolle.

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Food Frequency Questionnaire

Die folgende Liste enthält selenreiche Lebensmittel, die großteils aus Österreich stammen. Bitte geben Sie an, wie oft Sie diese im Verlauf der letzten drei Monate durchschnittlich gegessen haben und auch wie groß ihre durchschnittliche Portionsgröße ist (normal=1, mittel=1,25, groß=1,5). Wenn Sie bestimmte Produkte einer Lebensmittelgruppe unregelmäßig essen, antworten Sie bitte zu dem Produkt, das Sie am häufigsten essen.

Bitte markieren Sie pro Lebensmittel die Angabe, die am ehesten für Sie zutrifft, d.h. eine Markierung pro Lebensmittel.

Lebensmittel	**>1/d**	**1*/d**	**>4*/w**	**2-4*/w**	**1-2*/w**	**2-4*/m**	**1*/m**	**~3-5*/y**	**nie**	**Portions -größe**
Vollkornbrot										
Weizenbrot										
Müsli										
Pistazien										
Paranuss										
Eier										
Geflügel										
Schweinefleisch incl. Wurstwaren										
Rindfleisch										
Innereien: Leber										
Milch										
Süßwasserfisch										
Shrimps										
Seefisch										
Hülsenfrüchte (Bohnen, Erbsen, Linsen)										
Sojaprodukte										

Vielen Dank für die Mitarbeit!

Questionnaire I – General and medical data

Name, birthdate	Age
High, weight	(cm), (kg)
Family anamnesis in regard of thyroid	1st relatives = 1, 2nd = 2, no = 0
Thyroid dysfunction since ...	... months
Intake of OCP	yes= 1, no= 0, others = 2
Pregnancy: actual/ last deliv./ PP thyroiditis	yes=1, no=0/ ...months ago/ yes=1, no=0
Type of thyroid dysfunction	Hashi = 1, Base =2, deQuervain= 3
Type of thyr. dysf. before+after med. Treatment	Hyper=2, Hypo=0, Eu=1
Thyroid cancer	yes =1, no =0
SONOGRAPHY: Echogenicity	Echo-poor=1, -rich=2, normal=0, inhomog.=3
Struma nodosa	one=1, multi=2, no=0
Sum of thyroid volume	(right+left)
SCINTIGRAPHY:	Normal =0, abnormal =1
Nodules	Cold = 0, warm =1, hot =2
LABORATORY I + II: data before + after treatment	fT_4, fT_3, TSH, a-TPO, a-Tg, TRAK, neg. Ab
Status after operation	yes =1, no =0
Blood selenium level	µg/l; whole blood
Other diseases: colitis/ vitiligo/ rheuma	yes=1, no=0
Diabetes, hypertension, osteopor., elev. cholesterol	yes =1, no =0
Metabolic diseases, allergies, chron.gastritis	no=0; allergy=1, histam.- =2; fruc/ lac-intol. =3; gastr.=4
Other cancers	yes=1, no=0
Taken drugs (amiodarone/ interferon)	amiodarone=1, interferon=2
Intake of thyroid hormone-drugs	Euthyrox=1, Thiamazol=2, Thyrex=3, no=0
Under medical treatment (data of Sono, Szi, Lab)	since about … months (till Dez. 09)
Taking any other pharmaceuticals	yes=1, no=0
Time of thyroid operation	before … months (Dez. 09)
Further questions	Week of pregnancy = 1.(week), breast feeding=2, radio-iodine-therapy=3, Parkinson's disease=4, endocrine orbitopathie=5, asthma=6, anaemia=7, fat-tissue-inflammation=8, Psoriasis=9, sinusitis=10, Myasthenia grav.=11, Euphoria variegata=12

Questionnaire II – Nutritional habits

Feeding change	yes =1, no =0
Weight change	no =0, gain = 1, loss = 2
Vegetarian (or other nutrition forms)	yes=1, no=0
Daily fruits and vegetables?	yes=1, no=0; only 1 of them = 2 -> fruits=2.1, veg.=2.2
Nutrition is more ...	protein= 1, carbohydr.= 2, balanced =3
Largely regional products?	yes= 1, no = 0
Number of used vegetable oils	.....
Iodine elimination	yes=1, no=0
Eating iodine-containing food (seafood, algae)	yes=1, no=0
Eating cabbage products?	yes (monthly) =1, daily/weekly =2, no=0
Eating soy products?	yes= 1, no = 0
Alcohol drinking habit	daily = 1, weekly =0,14, monthly = 0,03, no = 0
Beer drinking habit	yes= 1, no = 0
Coffee consumption	0-2= 0 (low), 3-5= 1 (moderate), >5 cups /d= 2 (high consump.)
Tea consumption	yes= 1, no = 0
Eating daily chocolate/ -containing foods?	yes= 1, no= 0
Smoking habits	yes =1, no = 0, stopped smoking= 2
Doing sports regularly?	yes=1, no =0
Daily drinking amount (e.g. water, juices)	(in liters)
Number of Se deficiency symptoms	see below

Selen-Mangelerscheinungen	**Ja**	**Nein**
Myopathien		
Nagelveränderungen wie weiße Flecken		
Dünne und blassere Haare		
Gewichtsverlust		
Darmträgheit		
Depressionen		
Reizbarkeit		
Konzentrationsstörungen		
Immunschwäche		

Curriculum Vitae

Personal Details

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Date of birth:	November 4th, 1983
Place of birth:	Vienna
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Education

09/94 – 07/02	Bundesgymnasium Gänserndorf/ Franklinstr. 26, Vienna

Further Education

10/02 – 10/08	Degree studies of Nutrition Sciences, Department of Nutritional Sciences, University of Vienna Master Thesis: “Untersuchungen zum Duft Wiener Kaffeehäuser”
10/2009 –	Doctoral studies on the Department of Nutritional Sciences, University of Vienna, Wilhelminenspital; Doctoral Thesis: “Selenium and immune mediated diseases of the thyroid”

Work Experiences

07/02 – 08/02	Practical training by Erste Bank, Vienna
06/03 – 08/03	Practical training by Anker Snack & Coffee, Gastronomiebetriebs GmbH
06/04 – 08/04	Practical training by Anker Snack & Coffee, Gastronomiebetriebs GmbH
09/07 – 10/07	Practical training by MA 38-Lebensmitteluntersuchungsanstalt, Vienna
08/07 – 06/08	Project cooperation of WWTF „Haptic and Olfactory Design“

Professional Experiences

10/08 – 09/10	Promotor of P&R Marktservice, Schattenberger& Augustin GmbH
02/11 –	Obesity- and diabetes consultant, in cooperation with a general practitioner, AEGNUS Ernährungskonzepte GmbH: MyLine

Further Education

05/08	*Diplom-Coffee-Expert,* adult education center (VHS) Hietzing
11/08 – 06/09	Graduated nutritional consultant, Vitalakademie, graduated with distinction
06/09	*Coffee-Sommelier,* adult education center (VHS) Hietzing

Skills and Qualifications

Languages:	German, native language
	English, advanced
	French, basics
Computer:	MS Office 2007 (Excel, Word, Power Point)

Advanced training courses, University of Vienna

12/09	TS Workshop: Introduction in doctorate, DoktorandInnenzentrum, Vienna
01/11	SE Application training
06/11	SE Presentation techniques – How to find his own style

Publications

Publications

Diplom thesis „Untersuchungen zum Duft Wiener Kaffeehäuser “: WETZ, A.: Dem Kaffeehausduft auf der Spur, Die Presse, Wissenschaft, 13. Aug. 2009: Publication of the results of the Master Thesis

Dissertation „Selenium and immune mediated diseases of the thyroid", in preparation

Presentations at Scientific Meetings

Doctors' conferences of Merck GesmbH, Hotel Marriott Vienna, October 2009, topic: "Nutrition and the thyroid"

Congress in Barcelona, Poster presentation of provisional results of the dissertation topic, 2010

Interests

Sport: Jogging, Nordic Walking, Biking, Hiking

Others: Nutrition& Health, current research, culture, reading

Vienna, March 2011