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**Iodine deficiency in dogs and cats in EU countries**

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**Summary**

The objective of this thesis is to provide information on canine and feline iodine deficiencies in different European countries, with regards to the different diseases associated, along with their symptoms and clinical.

Data used in this review was obtained from previous studies, published in scientific journals, investigating iodine intake and its importance. Articles from human medicine were also used for the purpose of this review.

It was concluded that an ideal treatment protocol does not exist, although various measures can be taken, each with different extend of efficacy, to prevent iodine deficiencies.

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1. **Introduction** 
   1. **Iodine as an element on earth.**

Iodine is a micronutrient of crucial importance, with a relative atomic mass (atomic weight) of 126, 9. Before 1961, there was a relative scale based on the atomic mass unit a.m.u. (Zimmermann, 2009). It is mostly found in the thyroid gland, as it is a major constituent of thyroid hormones, while it also serves to support the development of the neural system (Farhana and Ganie, 2010; Taylor et al., 2014). It is mostly required at fetal life, as well as during early childhood in humans. Its intake depends on the diet e.g. vegetables that grow in iodine-rich environment, specifically in water and soil (Ikeda et al, 2000). Iodine is found worldwide but is unevenly distributed in the environment (Eastman and Zimmermann, 2014).

Iodine was discovered mainly by two scientists: Bernard Courtois and Gay-Lussac. Courtois had added sulfuric acid to the ash while he was burning seaweed and noticed the formation of violet vapor. Courtois then sent the crystals to Gay-Lussac who identified a new element - iodine (from the Greek word for violet) (Zimmermann, 2008).

Iodine should be distributed in foods, water and soil. Mc Clendon stated: “it seems possible that goiter maps and iodine maps, supposing they existed, would fit like the land fits the ocean, goiter incidence and iodine varying inversely” (Schlumberger G., 1955).

As stated by Lyn Patrick “The oceans are the worldwide repository of iodine” (Lyn Patrick, 2008). Iodine can be found in soil after volatilization from ocean water, by means of ultraviolet radiation. Soils near beaches contain higher iodine concentrations. However, when iodine concentrations are high in the ground, iodine binds strongly to the soil, resulting in vegetables having lower iodine content (Lyn Patrick., 2008). Therefore, crops in coastal areas grow in iodine deficient soil (Farhana and Ganie., 2010). Another reason why crops in coastal areas are iodine deficient can be due to the slow and incomplete cycle of iodine (Zimmermann, 2009). Normally it oxidizes from seawater and drops on land with the rain (Zicker and Schoenherr., 2012). However, in coastal areas, it does not return back to the soil (Zimmermann, 2009).

Iodine concentration is highest in seawater and marine fish (Zicker and Schoenherr, 2012). It is also high in milk and bread; however, boiling and baking may result in a small lose of iodine. As far as milk is concerned, the use of iodophors in the dairy industry for cleaning the equipment, as well as the teats before milking, may increase the iodine content in milk (Eastman and Zimmermann, 2014).

**2. Iodine in the organism.**

**2.1. Mechanism and metabolism of iodine**

Iodine in the environment can be found in various forms including inorganic sodium, potassium salts, inorganic diatomic iodine and organic monatomic iodine. (Lyn Patrick, 2008).

There are two forms of iodine that are absorbed through the intestinal tract: molecular iodine, which is transported by facilitated diffusion and iodides, which are absorbed by the sodium-iodide symporter (a transport protein in the gastric mucosa found on the apical surface of enterocytes). This symporter is found in different tissues such as the thyroid, mammary tissue, salivary glands and the cervix (Lyn Patrick, 2008).

Iodine is incorporated into thyroid hormones but it can also be “organified into anti-proliferative iodolipids in the thyroid” (Daminet and Duncan, 2003). Inside the follicular cells of thyroid gland, 4 atoms of iodine give one molecule of thyroxin and 3 atoms give one molecule of triiodothyronine (Lee et al, 2015). Epithelial follicular cells take up thyroglobulin by pinocytocis in colloid droplets and thyroid hormone secretion begins. Thyroglobulin will then be degraded by lysosomal proteolytic enzymes to produce iodothyronines (T3 and T4). The ratio of the thyroid hormones stored in the gland is 12:1 (T4:T3) (Daminet and Duncan, 2003).

Iodine is absorbed in the stomach and small intestines (duodenum) in the form of iodide (Venturi, 2009). It is ingested in the form of iodate or iodide (Kapil, 2007). The intake happens through food, drugs and water or from the deiodination of thyroid hormones (Fountoulakis et al, 2007). It is then absorbed in the mucosa of intestines by sodium –iodide symporter (Zicker and Schoenherr, 2012). Oxidative metabolism provides energy for this process (Fountoulakis et al, 2007). It is then transferred to the blood circulation and it is taken up by the kidneys and the thyroid glands. The sodium-iodide symporter (NIS) is found also on the thyroid follicular cells and they are responsible for the accumulation of iodide (Zicker and Schoenherr, 2012).

Excretion of iodine from the organism occurs through milk, urine, saliva and in feces (Fekete et al., 2008). Thus, urinary iodine (UI) is used for the expression of iodine concentration (micrograms per liter) related to creatinine excretion (Zimmermann, 2009).

Excretion is higher if there is increased iodine consumption. Iodine which is secreted in milk is very important during lactation for the newborns (Zicker and Schoenherr, 2012).

Mammals have a system for recycling iodine via gastro-intestinal tract and oral-salivary tract, which makes them more resistant against iodine deficiency (Ventury, 2009).

Premature animals require higher iodine intake because their iodine regulating mechanism is immature. When the animal is pregnant the requirement for iodine is four times higher (Riviere et al, 2009).

**2.2. Synergism with Selenium**

Like iodine, selenium can also be found in soil and hence in plants that grow in this soil (Peterson, 2012). It acts as an antioxidant and can protect the thyrocytes from hydrogen peroxide during the biosynthesis of thyroid hormones (Rasmussen et al, 2011).

Selenium and iodine are in the group of elements which are beneficial for health and they both take part in the regulation of thyroid gland functions (Smolen et al, 2016). Thus, selenium deficiency may also cause thyroid dysfunction and hypothyroidism (Peterson, 2012). The deficiency can cause an accumulation of peroxides which will damage the thyroid, while the concurrent deficiency of deiodinase will impair the formation of thyroid hormones (Eastman and Zimmermann, 2014). Selenium can be synergistic with iodine, as it can “affect both thyroid hormone homeostasis and iodine availability” (Cann et al., 2000).

If there is iodine and selenium deficiency and selenium is supplemented, it will cause the serum T4 to decrease. In turn, the iodine deficiency and hypothyroidism will be worsened (Cann et al., 2000). There is restoration of type I deiodinase activity that will normalize T4 deiodination; however, T4 synthesis still remains impaired due to the iodine deficiency (Eastman and Zimmermann, 2014). Thus, T4 cannot be converted to the active T3 in case of Selenium deficiency (*See Table 1*) (Rasmussen et al, 2011).

**3. Importance of iodine**

**3.1. Functions of iodine.**

Iodine is very important for maintenance of life in vertebrate animals (Zicker and Schoenherr, 2012). It is critical during pregnancy, due to neural development of the fetus, as well as during lactation as it maintains homeostasis in the mother and fetus (Luton et al, 2011; Versloot et al, 1997). Moreover, it helps in the maintenance and functioning of breast tissue and serves as an antioxidant (Lyn Patrick, 2008). Its deficiency can cause physical and mental problems (Versloot et al, 1997).

Iodine also plays a role in the immune function and in T3 and T4 synthesis (Farhana and Ganie, 2010). It directly acts to stimulate the cells of the immune system, like macrophages and dendritic cells (Fountoulakis et al, 2007). Furthermore, it plays an essential role in salivary glands physiology and in oral mucosa - it helps in tongue and salivary gland formation glands during embryogenesis by taking part in the initiation of metamorphosis, during which the salivary glands derive from I-concentrating oral cells. Moreover, during metamorphosis of amphibians, iodides, together with thyroxin, are also essential for the induction of apoptosis of the cells of tail, fins and gills. “Inorganic iodide appears to be necessary for all living animal cells” (Venturi, 2009).

Iodine is not only responsible for the biosynthesis of thyroid hormones but it can also regulate the function and growth of the thyroid gland. Thyroid hormones are responsible for the regulation of the function of different tissues in the body, especially brain and bone development (Castillo et al, 2001).

In a research conducted by Ren et al (2007) it was concluded that iodine “has beneficial effects on bone, cartilage, growth plate and chondrocyte differentiation in rats as well as Selenium” (Venturi, 2009).

Iodine can have anti-inflammatory and antioxidant properties. It also has anticancer properties including prevention of breast, thyroid and gastric cancer (Peterson, 2012). It is also the most important element against brain damage (Benoist et al., 2008). Its antioxidant properties are owed to the fact that hydrogen peroxide, catalyzed by thyroid peroxidase, oxygenates iodide to iodine, leading to the formation of thyroid hormones T3 and T4. Thus, the higher the iodine intake, the more hydrogen peroxide is used up in the aforementioned process whereby iodine acts as an antioxidant (Smyth, 2003).

An average-sized cat should be kept on a diet containing 25-100μg iodine per day (Peterson, 2012). As far as dogs are concerned, minimum iodine requirement in is 0,70 mg/kg diet (Wedekind et al, 2009).

Research conducted by Mumma et al showed that iodine concentration in cat foods ranged from 1,0 to 36,8 mg/kg dry weight. Iodine content in cat foods comes from different plant and animal sources, especially ocean fish (Mumma et al, 1986).

**3.2. Relationship with thyroid gland and thyroid hormones.**

“Two thirds of the total body iodine content can be found in the thyroid gland” (Fekete et al, 2008). In the body, the only iodinated organic compounds are the thyroid hormones. Thyroxin contains 65% iodine and 3,5,3-triiodothyronine contains 59% ( Riviere et al, 2009). When there is an iodine deficiency, the plasma T4 concentration decreases while T3 concentration is unchanged (Versloot et al, 1997). This is because T3 is more biologically active than T4 thus its increased production can maintain normal levels of thyroid hormone bioactivity in case of iodine deficiency despite the reduction in T4 (L Lee et al, 2015).

T3 contains three iodine atoms per molecule, whereas T4 contains four iodine atoms per molecule (Peterson, 2012). Sir Charles Harrington was the first to report that iodine makes up a major part of thyroxin (T4) (Smyth, 2003). During human pregnancy, there is an increase in T4 binding globulin and in the total plasma T3 and T4. However, at the end of gestation, T4 decreases (Versloot et al, 1997). The iodine requirement is higher due to the increase in maternal T4 production for the maintenance of maternal euthyroidism and the transport of thyroid hormone to the fetus before the fetal thyroid begins to function in the first trimester. In later gestation, it also needs to be transported to the fetus and, during this phase of pregnancy, there is high renal clearance of iodine (Zimmermann, 2009).

Hormones of the thyroid gland are responsible for the control of metabolic processes in most cells and the regulation of growth and development of most organs especially the brain. In humans, brain development occurs during fetal period. Therefore, low iodine intake in either this period or during the first two to three years of life, results in hypothyroidism and brain damage (Andersson et al, 2007).

When there is low iodine intake, thyroid hormones may still be adequately secreted due to the adaptive processes, which include the stimulation of the trapping mechanism of iodide by the thyroid, as well as the intrathyroidal metabolism of iodine occurring after that, which leads to the synthesis and secretion of T3. This mechanism is initiated by TSH secretion from the pituitary gland (Andersson et al, 2007). Therefore, both the intrathyroidal and extrathyroidal mechanisms respond to maintain normal function of thyroid and help for the elevation or maintenance of T3 at physiological levels (Obregon et al, 2005).

TSH controls thyroid function by stimulating thyroid hormones synthesis and secretion. Thyroid follicular cells have a basolateral membrane where TSH binds on the receptors and activates the intracellular signaling pathways for the regulation of growth and cell function of thyroid gland (Fountoulakis et al, 2007). Thus, TSH can stimulate each cell to increase the uptake of iodine and the consequent synthesis and secretion of thyroid hormones. Thyroid hormones are then deiodinated in the liver and iodine is released in the circulation to be taken up again and be reused by the thyroid gland (L Lee et al, 2015).

Iodine entry in the cells of the thyroid gland is very important for thyroid hormone synthesis (Fountoulakis et al, 2007). Thyroid hormones are essential for various vital physiological processes, such as protein synthesis, glycogenolysis, nitrogen retention, lipolysis, absorption of glucose and galactose from intestines, as well as the uptake of glucose by adipocytes (Kapil, 2007).

The sodium-iodide symporter allows for the iodide uptake in the thyroid gland, therefore defects on the symporter may potentially cause goiter (Bojanic et al, 2011). This is an active process regulated by TSH and the blood flow to the thyroid (Versloot et al, 1997).

The first step in iodine metabolism is the iodine trapping (Farhana and Ganie 2010). This occurs by plasma iodide being actively transported into the thyroid (R F Hurrell, 1997). Following trapping, synthesis and secretion of thyroglobulin take place. Lastly, iodide is oxidized to iodine which will then be used to synthesize the thyroid hormones.

**4. Iodine deficiency**

In 1990, the World Health Assembly started a resolution for the elimination of iodine deficiency in both animals and humans. This was restarted in 1998, 2003 and 2007 (Andersson et al, 2007). It has been estimated that 29% of the world’s population lives in deficient areas. The regions being primarily affected are the Himalayas, the European Alps and the Andes due to iodine being washed away by glaciations and flooding. Africa and Eastern Europe are also considered deficient due to the long distance away from the oceans (Lee et al, 2015).

So far, apart from underdeveloped countries, like Africa and EU countries, UK has reported the highest number of cases of human iodine deficiencies (Patrick, 2008; Taylor et al., 2014). Hungary is also amongst the highly deficient countries in Europe but the region of Debrecen is an exception. Multivitamin tablets containing iodine and iodized salt are available for the public. Brussels and southwest France are also iodine deficient but only to a limited extent (Mezosi et al, 2000).

In an experiment conducted by Castillo et al., it was proved that puppies consuming commercial and home-prepared diets were deficient in iodine, basal serum thyroxin and free thyroxin. However, the excretion of urinary iodide and thyroid releasing hormone was higher in the group of puppies being on commercial and home-prepared diets (Castillo et al, 2001).

**4.1. Causes of iodine deficiency.**

**4.1.1. Inadequate intake.**

Iodine deficiency can be due to inadequate intake or inadequate utilization. An inadequate intake can be due to low intake of food with high iodine content, like seafood, whereas inadequate utilization refers to the failure of proper metabolism of iodine which can be due to various causes, for example the presence of goitrogens in certain foods (Farhana and Ganie, 2010).

Low iodine intake occurs when the amount in soil is very low, which consequently leads to low concentration of iodine in food products. Intensive cropping and use of alkaline fertilizers can also result in decrease iodine content in the soil (Kapil, 2007).

Diets that have higher or lower iodine content as well as fluctuations in the amount of iodine are not recommended (Peterson, 2012). According to a research in the USA, iodine concentration in canned foods may increase or decrease away from the optimum recommended value. It also varies according to packaging types, brands, iodine supplementation type, seafood ingredients and intended use, but overall the consumption of canned foods is more likely to lead to iodine deficiency and, in turn, thyroid hyperplasia (Edinboro et al, 2013).

During pregnancy, iodine deficiency in the mother will result in iodine deficiency in the fetus, leading to congenital abnormalities, abortions and stillbirths (Delange et al, 1993).

**4.1.2. Goitrogens.** (*See table 1)*

Goitrogens are chemical substances that interfere with thyroxin synthesis. They are found in plant food and drinking water (Kapil, 2007). There are two groups of goitrogens: those acting directly and those acting indirectly on the thyroid gland. Goitrogens directly affecting the thyroxin synthesis act by inhibiting the transport of iodide into the thyroid gland, while goitrogens acting indirectly inhibit the “intrathyroidal oxidation and organic binding process of iodide” which can interfere with proteolysis and hormone release (Eastman and Zimmermann, 2014).

Furniture, plastics, electronics and textiles have a fire-retardant substance called Polybrominated Diphenyl Ether which is transferred with dust on the floors. Cats that live indoors and lay down on the floor can collect this substance together with dust during grooming (Peterson, 2014). Polybrominated Diphenyl Ether increases the biliary elimination of thyroid hormones (Peterson M, 2012).

Other goitrogen substances include the flavorings contained in canned food, as well as the plastic linings in easy-open lids which may contain a thyroid disruptor substance (bisphenol-A). In addition, goitrogens like soy-isoflavones may be present in the material of the lids, which can inhibit thyroid peroxidase in thyroid follicles. This results in the decrease of T4 and T3 synthesis. In case of pre-existing iodine deficiency, the soy’s antithyroid effects are further enhanced, resulting in goiter (Peterson, 2012).

Upon ingestion of goitrogens belonging to Brassica species, including cabbage, Brussels sprouts, turnip, as well as cassava, severe impairment in thyroid hormones synthesis may be caused. Goitrogens can also be found in milk if livestock is grazed on goitrogen-containing plants. The major groups of goitrogens that may be found in plants are glucosinolates. There are two main categories of glucosinolates: those producing thiocyanates, which block the transport of iodine into the thyroid gland and those producing oxazolidine-2-thiones, which prevent the iodinization of thyroglobulin. Thiocyanates can be found in cabbage, radish and cauliflower and act by competing with iodide for uptake into the thyroid (Hurrell, 1997). Thiocynates may not only be ingested by animals but also inhaled from the household environment through second-hand cigarette smoke (*See table 1*) (Riviere et al, 2009). In Africa there was evidence that the high consumption of insufficiently processed cassava leaves impairs the iodine absorption and utilization from the thyroid gland. These leaves contain constitutes that release cyanide after hydrolysis, which is then converted to thiocyanate after ingestion (Fountoulakis et al, 2007)

Goitrogens such as flavonoids, pyridines, organochlorines and polycyclic aromatic hydrocarbons can affect the iodine level in food (Eastman and Zimmermann, 2014). The action of bisphenol-A (BPA) can be potentiated by the simultaneous presence of iodine deficiency. BPA is present in the inner lining of metal cans and serves for the maintenance of food quality and taste. BPA structure is similar to thyroid hormones, which is the reason why it has a toxic effect on thyroid function (Peterson, 2012).

According to a research conducted on rats, a soybean based diet can induce goiter and thyroid carcinoma due to iodine deficiency, while there is an increased loss of T4 in the feces (Ikeda et al., 2000).

**4.1.3. Nutrient interactions.**

Thyroid hormone synthesis does not solely depend on adequate levels of iodine – other micronutrients also play a key role in thyroid metabolism. For example, in case of selenium deficiency, the conversion of T4 to T3 in the liver does not happen because selenium is part of the deiodidase enzyme. Iron is also similarly important, which has been proved by studies conducted on animals and humans, revealing that iron deficiency can impair thyroid metabolism and influence iodine deficiency disorders (Zimmermann et al, 2000). Furthermore, in deficiency of vitamin A there is also impairment of thyroid hormone production (See *figure 1*) (Hurrell, 1997).

Inadequate intake of iron reduces heme-dependent thyroid peroxidase (TPO) activity in the thyroid gland while vitamin A deficiency increases TSH stimulation and the range for goiter formation is higher due to the suppression of the pituitary TSH β gene (Zimmermann, 2009). In Africa there is a big problem with iodine deficiency correlated with iron deficiency anemia. Thyroid hormones synthesis requires catalyzation by thyroperoxidases, which depends on iron. Therefore, iron deficiency may result in low plasma thyroxin and triiodothyronine, as well as I reduced rate of conversion of T4 to T3 (Zimmermann et al, 2000).

**4.2. Symptoms of iodine deficiency.**

Inadequate iodine intake can cause goiter, hypothyroidism and cretinism, increases the mortality and reduces growth (Taylor et al., 2014). Moreover, iodine deficiency may result in benign pathological breast tissue growth/formation in animals and humans since iodine has an anti-tumor effect which is absent in case of deficiency. This anti-tumor effect of iodine can potentially “soften” tumors and reduce nodulation (Cann S.A., et al, 2000). It can also cause autonomous nodular growth and regulate the function of the gland and this is the most common cause for hyperthyroidism (Laurberg et al, 1998).

During pregnancy, iodine deficiency causes cretinism which “is the world’s most common preventable cause of mental retardation” (Xue-Yi et al, 1994). The low iodine intake can cause hypothyroxinaemia which results in the low transfer of thyroxin transplacentaly during the first and second trimesters (Andersson et al, 2007). It can be prevented with iodine supplementation before conception. Cretinism in animals and humans, caused by iodine deficiency, is characterized by deaf-mutism, intellectual, rigid spastic motor disorder and sometimes hypothyroidism (Xue-Yi et al, 1994). It can cause abortion and stillbirth in pregnant women (Venturi, 2009). Spastic diplegia, hearing defects and strabismus are some of the findings in neurologic endemic cretinism (Andersson et al, 2007).

Low plasma iodine leads to a decrease in circulating thyroid hormone concentration which causes the pituitary gland to increase its secretion of TSH. This in turn leads to goiter and thyroid hyperplasia. When the TSH level is higher, hydrogen peroxide is produced, causing oxidative stress (Smyth, 2003).

After a period of low iodine consumption, increased consumption via food or water can cause human thyrotoxicosis (Edinboro et al, 2004).

In production animals, iodine deficiency can cause stillbirth, abortion, fertility problems and congenital goiter as well as myxoedema (Fekete et al, 2008). In humans it can cause orthography problems (Taylor et al, 2014).

Abnet et al. and Dye et al. revealed a relationship between iodine deficient goiter and gastric cancer (Venturi, 2009). In severely iodine deficient children, learning ability, memory and verbal and perceptual performance are impaired and the motivation is lowered (Tiwari et al, 1996).

**4.3. Iodine deficiency disorders.**

**4.3.1. Hypothyroidism.**

The most common thyroid dysfunction in dogs is hypothyroidism, while in cats its hyperthyroidism (Zicker and Schoenherr, 2012). Hypothyroidism may result from lymphocytic thyroiditis or thyroid atrophy (Rand et al, 1993). The causes can be due to environmental or genetic factors, such as enzymatic defects, which can impair the synthesis of thyroid hormones, or mutations of genes acting on thyroid cells (Fountoulakis et al, 2007). When there is low iodine intake, the level of thyroid hormones in the blood decreases, which results in hypothyroidism. A high intake of iodine also impairs thyroid hormone biosynthesis and growth, also resulting in hypothyroidism (Castillo et al, 2001).

Hypothyroidism can be differentiated according to the place of the defect on the hypothalamus-pituitary-thyroid (HPT) axis: “primary (thyroid), secondary (pituitary) or tertiary (hypothalamus)”. Based on the time of onset, hypothyroidism can be congenital or acquired (Bojanic et al, 2011). It is most commonly found in adult dogs, of 7 years old on average.

Primary hypothyroidism can be caused by thyroid destruction. It is characterized by a defect directly affecting the thyroid, for example neoplasm, infection, surgery and iatrogenic (thyrotoxic drugs). In more than 95% of hypothyroid dog cases are due to primary hypothyroidism. Secondary hypothyroidism refers to malfunctioning of the pituitary, due to, for example, tumors (Finora and Greco, 2007). It is characterized by low TSH secretion of the pituitary gland due to destruction, neoplasia or infection but it is a rare condition (Meeking, 2005).

Clinical signs of hypothyroidism in dogs include lethargy, increased body weight, alopecia, pyoderma and seborrhea (Zicker and Schoenherr, 2012). Alopecia is usually bilaterally symmetric and first starts at the lateral trunk, ventral thorax and tail. Also, dry scaly skin, ceruminous otitis, hyperpigmentation and poor wound healing can be observed. In dogs with hypothyroidism due to iodine deficiency, there is no decrease in libido or sperm quality (Scott-Moncrieff, 2007). Presence of alopecia on the head and extremities is not pruritic and polyuria and polydipsia are absent. The signs of alopecia do not depend on the sex of the animal. Changes in respiration of the dog can also be found due to changes in the connective tissue of pharynx and larynx. Research conducted by Andre et al indicated that hypothyroidism can be associated with neuromuscular signs, like vestibular deficits, lower motor neuron signs, mega esophagus and laryngeal paralysis (Jaggy et al, 1994). It can result from segmental demyelination, accumulation of mucopolysaccharides, cerebral atherosclerosis, axonopathy or hyperlipidemia (Meeking, 2005).

Adult-onset hypothyroidism in cats results in obesity, lethargy, cold intolerance and dermatological problems, for example “puffy” face. Increased blood albumin and calcium, hyperkeratosis, dry and dull hair coat, poor appetite and lighter colored undercoat can be found. It can be diagnosed with thyroid-stimulating hormone test and thyroid biopsy (Rand et al, 1993).

Hypothyroidism in humans can also be caused by an autoimmune disease called Hashimoto’s thyroiditis and this disease in dogs corresponds to the so called canine lymphocytic thyroiditis. In case of this autoimmune disease, there is infiltration in the thyroid gland by B and T lymphocytes, as well as destruction of the normal follicular structure of thyroid, due to the action of circulating antibodies present against thyroglobulin (Bianchi et al, 2015). Thyroglobulin is the protein found in the colloid of the thyroid follicles where thyroid hormones are stored (Roitt et al, 1957). Thyroid idiopathic atrophy may also cause hypothyroidism through a degenerative process and it is thought to be the end stage of canine lymphocytic thyroiditis (Bianchi et al, 2015).

In puppies, hypothyroidism is called cretinism. In case of cretinism, there is a shrunken thyroid gland, which is the opposite of goiter. Slow growth and problems in mental development are the main consequences. Clinical signs of cretinism include kyphosis, shortened limbs, gait abnormalities, alopecia, short skull, goiter and lethargy (Nelson and Couto, 2014).

Endemic cretinism is present in areas where there is severe iodine deficiency. It can be caused by thyroxin deficiency transmitted from mother to fetus in the period of midtrimester which results in neurological symptoms. Sporadic cretinism is caused be defective biosynthesis of thyroid hormones or by thyroid gland agenesis or dysgenesis (Lindholm and Laurberg, 2011). It is more severe than congenital hypothyroidism and is irreversible after birth. Symptoms include and are not limited to, loss of hearing, due to the damage in cochlear development (Obregon et al, 2005).

Hypothyroid mothers give birth to children with cretinism. This can be prevented by supplementing iodized oil before pregnancy, which can help in reducing the number fetal deaths (Delange et al, 1993; Hetzel, 2000).

Congenital hypothyroidism is infrequent in dogs and cats but it can also be caused by iodine deficiency. Clinical signs can be dwarfism, retarded growth and impaired mental status (Bojanic et al., 2011). In Toy Fox terriers, Giant Schnauzers and Abyssinian cats, congenital hypothyroidism (CH) with goiter was observed with clinical findings such as dwarfism (Fyfe et al, 2003).

Other clinical signs include anestrus, weakness and testicular atrophy. Malassezia and generalized demodicosis can be found in hypothyroidism due to impaired humoral immunity and T-cell function (Finora and Greco, 2007). Reproductive abnormalities are uncommon; however, silent estrus, prolonged bleeding, failure to cycle and improper lactation may occur.

It is very difficult to differentiate between hyperadrenocorticism and hypothyroidism. In hyperadrenocorticism the animal can have polyuria and polydipsia and low thyroid hormones (Peterson et al, 1984).

**4.3.1.1. High risk breeds for developing hypothyroidism.**

Purebred dog breeds are more sensitive to hypothyroidism than mix breeds due to genetic predispositions, usually in medium and large size dogs (Bianchi et al, 2015).

In a research conducted by Scarlett, it was concluded that dogs of high-risk breeds, are at risk until 2-3 years of age. Low-risk breeds of dogs are German Shepherds and mixed breed dogs; unlike high-risk breeds, these are at risk until 9 years of age.

High risk breeds include Chow-Chows, English bulldogs, Spaniels and Basenjis. Another study conducted in the USA, Doberman Pinschers, Great Danes, Poodles, Dachshunds, Schnauzers, Irish Setters and Boxers were 50% of the cases of hypothyroid dogs used for the purpose of the study (Scarlett, 1994). According to Bianchi et al, Rhodesian ridgeback, Gordon setter, English setter and the Beagle also belong in high risk breeds category.

A study conducted by Bianchi et al, examined three high-risk breeds: Gordon setter, Hovawart and the Rhodesian ridgeback. Three genes were found to contribute to the development of the disease: LHFPL5, SRPK1 and SLC26A8 genes. It was concluded that breeding programs could potentially result in more resistant breeds, thus decreasing the likelihood of dogs developing an iodine deficiency (Bianchi et al, 2015).

**4.3.2. Goiter.**

Goiter is the non-neoplastic enlargement of the thyroid, the special gland without duct in front of the larynx in the neck. Goiter develops when there is thyroid hormone deficiency and this causes pituitary release of thyrotropin to increase (Fyfe et al, 2003).

When the condition is in areas close to each other is called endemic goiter (Carpenter, 2005). The range for endemic goiter is considered to be between 5-10% (Fountoulakis et al, 2007). A. Chatin was the first to state that iodine deficiency is the cause of goiter (Carpenter, 2005). This is because thyroid gland depends on the intake of iodine for the maintenance of plasma inorganic iodine in normal levels. This happens due to the lack of renal iodine homeostatic mechanisms (Fountoulakis et al, 2007).

Goiter formation involves follicular epithelial cells multiply and they form new follicles (Gerber et al, 1994). In humans, goiter means that on clinical examination, thyroid gland has a unilateral size bigger than his distal thumb phalange. It can be classified according to the morphology of the thyroid parenchyma- diffuse or nodular and to toxic or non toxic based on the functional status. Nodular goiter is then classified to uninodular or multinodular where multinodular means the appearance of “multiple polyclonal thyroid nodules that are structurally and functionally heterogeneous” (Fountoulakis et al, 2007). Thyroid nodules are formed due to somatic mutations after thyroid goiter in iodine deficient areas (Maier et al, 2007). This happens in adults where multinodular goiters are formed with autonomous nodules containing thyrocyte proliferation with scattered cell clones that harbor activation mutations of the TSH receptors (Andersson et al, 2007).

People who drink water from iodine-poor area will develop goiter that will disappear when they will travel to an iodine rich area (Lindholm and Laurberg, 2011).

According to Carlson (1914) canine and feline thyroid hyperplasia can be congenital. One of the most common symptoms of goiter is bilateral exophthalmous. Cats develop goiter less frequently thus they are less susceptible (Schlumberger G., 1955).

Marine conducted a study in dogs and concluded that in the development of goiter there is an increase in the blood flow as well as the dimensions and the number of epithelial cells. This cellular changes result after low iodine intake. She also stated that after removal of the gland during pregnancy, there will be enlarged thyroid in the puppies (Ross, 1921).

The minimum intake of iodine in order to prevent goiter is 1μg/kg body weight. According to Victor Horsley, eggs can help treat goiter (Lindholm and Laurberg, 2011).

In humans, toxic or exophthalmic goiter (opposite of myxedema) can occur with protruding eyeballs, decrease of weight, palpation of the heart and nervousness. This is called Grave’s disease (Carpenter, 2005). It is a thyroid autoimmunity and is caused by TSH stimulation of antibodies (Laurberg et al, 1998).

Goiter is more commonly seen in women than in men, likely due to hormonal differences especially during pregnancy (Knudsen et al, 2002). The most dangerous periods for goiter development are during puberty and pregnancy especially in the early stages (Ross, 1921). This is because during pregnancy, nutritional and energy demands are higher and the loss of iodine through urine is increased due to higher glomerular filtration rate (Knudsen et al, 2002).

According to McCarrison, goiter can also be caused by infection, likely facultative anaerobic bacteria that grow in the intestinal tract. Their toxins are absorbed and act on the thyroid gland. Barherd reported that in areas with poor sunlight goiter is more prevalent because sunlight has a sterilizing effect in the drinking water and it might help for the prevention of goiter (Ross, 1921).

**4.3.3. Hyperthyroidism.**

Hyperthyroidism was first diagnosed in the USA and nowadays is the most common disease that affects cats, especially female ones who develop it more often (Peterson, 2014). It is a form of thyrotoxicosis due to the increase production and secretion of thyroid hormones (Bahn et al, 2011).

It is characterized by enlargement of thyroid gland, increased concentration of thyroid hormones in the circulation and high uptake of iodine by the thyroid. It is caused by high secretion of thyroid hormones, thyroxin and triiodothyronine (Hoenig et al, 1982).

Hyperthyroidism or toxic nodular goiter in cats is increasing dramatically during the last years. “Hyperthyroid cat goiters contain single or multiple autonomously functioning and growing thyroid nodules” (Peterson, 2014). Therefore, hyperthyroidism in cats is similar histologically and clinically to toxic nodular goiter in humans. It is mechanistically different from Grave’s disease due to the independence of the function and growth of the nodules from extrathyroidal circulating stimulators (Peterson, 2014).

Hyperthyroidism in cats can be due to either excess or insufficient iodine levels and it’s the most common endocrinopathy (Ranz et al, 2002). It can be due to nutritional deficiencies or excess or thyroid-disrupting compounds that can be found in the environment, diet or drinking water (Peterson, 2012). The most serious cause of hyperthyroidism is adenomatous hyperplastic nodules (Hoenig et al, 1982) resulting from toxic nodular goiter due to increase intrinsic growth capacity of thyroid cells (Hans et al, 1987).

If a cat consumes food that is iodine deficient and later consumes a diet with excessive iodine it can result in clinical hyperthyroidism (Edinboro H. et al,. 2013).

In cats over 6 years of age, hyperthyroidism is very common. A study conducted by Edinboro et al assessed if the consumption of canned foods played a role in hyperthyroidism (Edinboro H. et al, 2013). Scarlett et al found that cats eating a high proportion of canned food are at a higher risk of hyperthyroidism (Scarlett, 1994) (*see figure 2)*. Feline hyperthyroidism can also be caused by increased iodine content in food (Edinboro et al, 2004).

Dietary flavonoids are found in cat foods and play a role in the development of toxic nodular goiter. Thyroid peroxidase activity is inhibited by flavonoids and they induce autonomous mitogenesis (Peterson, 2014).

Clinical signs of hyperthyroidism include polyphagia, weight loss, polydipsia/polyuria and gastrointestinal signs (Zicker and Schoenherr, 2012). Also poor hair coat, diarrhea, chronic vomiting, tachypnea/tachycardia and cardiac arrhythmias can be found (Scott-Moncrieff, 2012). (*See figure 3.)*

Subclinical hyperthyroidism is the low production of serum thyroid stimulating hormone (TSH) but triiodothyronine and free thyroxin values range to a normal level during subclinical hyperthyroidism (Bahn et al, 2011).

Benign pathological changes of the thyroid gland can be found in cats with toxic nodular goiter. About 2% of these cats develop thyroid carcinoma which is classified as papillary, follicular or mixed. Malignancy can develop if toxic goiter is not treated with thyroidectomy (Peterson, 2014).

**4.3.4. Myxoedema (severe hypothyroidism).**

Myxoedema is the generalized, peculiar non pitted swelling of the skin during hypothyroidism (Doliger et al, 1995).

Victor Horsley removed the thyroid gland from animals and showed that myxedema developed slowly. It is formed after dysfunction of thyroid gland (Lindholm and Laurberg, 2011).

Clinical signs include bradycardia, very low temperature, weakness of the animal, hypoventilation, hypotension and edema of the face and neck (Finora and Greco, 2007). Also dermal mucinosis or cutaneous vesiculation may be present (Doliger et al, 1995).

Myxedema coma can threaten the life of the animal and it is a rare endocrine emergency. Clinical signs include altered mental status and thermoregulation, non pitting skin edema, hypoxemia, hypoglycemia and hypothermia but without shivering (Finora and Greco, 2007).

It can be treated with thyroiodine, a substance rich in iodine in thyroid tissues that is present in both animals and humans (Lindholm and Laurberg, 2011). Thyroid hormones can be administered either orally or intravenously (Meeking, 2005).

**4.3.5. Tumor formation due to iodine deficiency.**

Amongst the most frequent endocrine malignancies, thyroid carcinomas are the most commonly present. The most frequent types are the differentiated forms (follicular, papillary or mixed papillary-follicular) (Feldt-Rasmussen, 2001).

The mechanism of iodine deficiency and thyroid tumor formation is defined as stimulation of follicular cells by increased serum thyroid-stimulating hormone following a reduction in thyroid hormone synthesis (Ikeda et al., 2000). When iodine levels fall lower than the recommended levels, the thyroid gland cannot synthesize enough amounts of thyroid hormones (Benoist et al., 2008).

Chronic iodine deficiency will decrease thyroxin levels. The pituitary responds by increasing thyrotrophic cells. As the time passes, the hyperplasia can lead to tumor formation.

The proliferation of normal thyrotrophs may induce nodular hyperplasia which is the first stage in adenoma formation. According to Bielchowsky, tumors of the thyroid may derive due to iodine deficiency in the diet. It is stimulated by the increased level of thyrotrophic hormone after a stimulus of the pituitary to produce it due to deficiency of thyroxin (Bielschowsky, 1953).

According to Schlumberger, thyroid carcinoma can metastasize in the lungs and thyroid and pulmonary veins. The most common type of thyroid tumor is adenocarcinoma (Schlumberger, 1955).

The Chernobyl nuclear plant catastrophe in Belarus leads to the contamination of food and water with iosotopes of radioactive iodine. As a result, animals and humans have suffered from thyroid cancer due to contamination of food and iodine deficiency in the environment (Gembicki et al, 1997).

After a long period with iodine deficiency, thyroid epithelial cell carcinomas can be formed. The types of thyroid carcinoma depend on the intake of iodine. The follicular, anaplastic and papillary carcinomas are more likely to be found in iodine rich areas. In iodine deficient areas, more benign nodules in the thyroid gland and more benign goiters are present.

According to Feldt-Rasmussen, breast cancer depends also on iodine intake and inorganic iodine showed suppressing effect of breast cancer.

In iodine deficient animals, malignancies such as follicular adenocarcinomas were found and hyperplasia was present due to overstimulation by TSH (Feldt-Rasmussen, 2001).

**5. Iodine deficiency in other animals**

**5.1. Iodine deficiency in fishes.**

Bonnet was the first to report thyroid hyperplasia in fish (trout and salmonidae) because of the high O2 requirement. Usually if a fish is raised in iodized water, it prevents thyroid hyperplasia (Schlumberger G., 1955).

**5.2. Iodine deficiency in amphibians and reptiles.**

Professor Dodd conducted a study on the appearance of goiter in amphibians. The results were perplexing since goiter had not appeared in amphibians other than the newt. He explained that it can be due to the introduction of thiocyanates from rabbit feces in ponds.

A study on reptiles indicated goiter was only present in 2 turtles and a lizard due to the low iodine in diet in the zoos (Lyn Patrick, 2008).

**5.3. Iodine deficiency in domestic mammals.**

“In regions where endemic goiter is common in man it is also prevalent among his domesticated animals” (Lyn Patrick, 2008).

**5.3.1. Cattle**

Goitre appears rarely in adult cattle, however, it is often present in newborn calves (Lyn Patrick, 2008). In Iceland they feed the cows with fish meal so the dairy products are high in iodine content. For this reason, the increasing rate of subclinical hypothyroidism is due to elevated intake of iodine because it can inhibit the thyroid gland (Laurberg et al, 1998).

**5.3.2. Pigs.**

Sows should take enough iodine from food in order to prevent looses of newborn piglets, otherwise they born hairless, myxedematous and stillborn (Lyn Patrick, 2008).

**6. Diagnosis and treatment of iodine deficiency in general.**

The total goiter prevalence (TGP) was used as indication for iodine deficiency but nowadays the urinary iodine (UI) is preferably used. (Benoist et al, 2008).

Measurement of whole blood, plasma or serum for iodine as well as urine sample is used (Cann S.A., et al, 2000). Diagnosis also includes the serum T4 concentration, complete blood count and biochemical profile. Hypokalemia and increased alanine aminotransferase and alkaline phosphatase are a typical biochemical finding (Scott-Moncrieff, 2012). Total T4 level measurement can be done with ELISA, chemiluminescence and radioimmunoassay (Kooistra et al, 2000).

In Ancient Greece, goiter was treated with marine sponge, ashed or seaweed (Zimmermann, 2008).

The route of administration of iodized oil should be taken into consideration in iodine deficiency treatments. When given orally, there may be an increase in the concentration of serum thyrotropin, thyroid autoantibodies production and necrosis of thyroid tissue. However there may be no effect on the goiter because “the iodized oil is rapidly deiodinated in the digestive tract” thus intramuscular administration might be safer. But, if the dose of iodized oil is low for oral administration it can be safe and practical (Tonglet et al, 1992).

Thyroid scintigraphy can be used to help in the diagnosis and treatment management of feline hyperthyroidism, canine hypothyroidism and canine thyroid carcinoma (Daniel and Neelis, 2014).

Thyroid disease is more difficult to diagnose in older animals because of the presence of any medication in serum, the age and illness. Different drugs (e.g. glucocorticoids) can cause changes in thyroid hormones concentration, thus leading to a wrong diagnosis (Daminet and Duncan, 2003).

In puppies, increasing the iodine content of diet can result in decreasing in total and free T4 (Daminet and Duncan, 2003).

If the iodine treatment happens up to the end of the second trimester it can protect the fetal brain. If the treatment takes place later in pregnancy or after delivery, it may improve developmental achievement and brain growth, but it does not improve neurologic status (Xue-Yi et al, 1994).

According to research, iodine deficiency has improved since 2003, but there are countries that may cause iodine-induced hyperthyroidism (Benoist et al, 2008).

**6.1. Diagnosis and treatment of hypothyroidism.**

TSH stimulation test and ultrasound can diagnose hypothyroidism. In hypothyroid dogs there is an increase of TSH concentration in plasma as well as low thyroxin concentration in blood and this can be used for diagnosis ( Kooistra et al, 2000).

Hypothyroidism can be treated orally with thyroid extract-thyroxin. Levothyroxine can be also given. For cretinism in humans, feeding whole glands and injection of extracts made from animal thyroid glands was one method used anciently (Carpenter, 2005).

**6.2. Diagnosis and treatment of hyperthyroidism (or toxic nodular goiter).**

The clinical examination of animal with toxic nodular goiter involves palpation of one or more thyroid nodules and along with the presentation of hyperthyroidism symptoms (Peterson, 2014).

Diagnosis of hyperthyroidism can be based on history, enlargement of thyroid and clinical signs (Daniel and Neelis, 2014). Weight loss is the main clinical sign despite the good appetite (Peterson, 2014). Also thyroid function tests, thyroid histopathology, thyroid scans and radioiodine uptake concentrations are compared with those in normal cats (Hoenig et al, 1982). The high serum concentrations of thyroxin and triiodothyronine are used for diagnosis of feline hyperthyroidism (Peterson, 2014).

For thyroid imaging it is important to check thyroid size and morphology ultrasonography, scintigraphy, computed tomography scans and magnetic resonance imaging can be used (Peterson, 2014).

Histopathological diagnosis of feline hyperthyroidism will reveal single or multiple hyperplastic or adenomatous nodules. The cell sizes and the volume of the nuclei are larger than the normal. Due to decreased storage of thyroglobulin there will be a faint staining with PAS in the colloid of toxic nodular goiter because of hypersecretion of thyroglobulin (Peterson, 2014).

Treatment of feline hyperthyroidism and toxic nodular goiter can be done by using radioiodine therapy (Daniel and Neelis, 2014). Other treatments include antithyroid drug therapy (like Methimazole and Carbimazole), surgical resection by removing the abnormal thyroidal tissue or dietary management. Radioactive iodine (I131) can be injected intravenously or subcutaneously and it is a safe method of treatment (Scott-Moncrieff, 2012).

Percutaneous ethanol can be used also or thermal ablation of the cat’s thyroid nodules (Peterson, 2014).

**7. Prevention of iodine deficiency.**

Prevention and control of iodine deficiency is crucial in areas where iodine concentration in diets fails to meet requirements (Andersson et al, 2007).

The prevention of iodine deficiency is very important because it is easier than the treatment, thus different prophylactic methods are used. A good way of prevention according to MacCarrison is good hygiene conditions, boiling of water before drinking and intestinal antiseptics for the bacteria growth (Ross, 1921).

In humans and animals the most widely used strategy to control iodine deficiency is universal salt iodization (USI). This means that the salt used for human and animal consumption is iodized (Benoist et al, 2008). Salt iodization was first adopted in 1993 by the World Health Assembly for the control of iodine deficiency. The first European country that introduced iodized salt was Switzerland. It is the easiest and cheapest method and was chosen due to the widespread consumption of salt. However, iodized salt is more expensive than non iodized salt therefore it is less used. In areas where salt iodization is not attainable and the rate of iodine deficiency is high, iodide or iodized oil is used directly. In Romania, the use of iodized oil is obligatory in areas with very low iodine intake. This helps for the minimize of goiter from 29% to 9%. In Finland, iodine has been added to animal fodder and fertilizers so the iodine content in food of animal origin has increased. In farms, salt licks containing iodine can be also added to increase the sources of iodine (Andersson et al, 2007).

Iodine can be found in salt in the form of potassium iodide (KI), potassium iodate (KIO3), or sodium iodide were iodate salt is preferred which is easier to be storage. In EU countries, bread that contains iodine is used recently. Bakeries also use potassium iodide as an ingredient. Iodized water or tea has also been used also in some countries (Andersson et al, 2007). Sometimes, dough conditioner containing iodate was used for making bread. Erythrosine is a red coloring product use in food production, cosmetics and pharmaceuticals high in iodine content (Zimmermann, 2009).

In countries like United States of America there is a control program against iodine deficiency disorders (IDD), reducing the rate of iodine deficiency. However in Europe compare to other countries there is a huge problem with the salt iodization that reaches only 27% of households. Unfortunately, in farming and food processing iodization of salt has not been adopted by European national governments (Andersson et al, 2007).

Improving iodine content in farm animal food has several beneficial effects including an increase in live births and weight gain. In addition there is an improvement in the general health and strength of an animal, the wool quality of sheep, the meat quality in cows and a decrease in congenital abnormalities (Andersson et al, 2007).

In humans, the daily intake recommended of iodine is 150 μg (Eastman and Zimmermann, 2014). The salt should be packed in a waterproof bag with polythene lining to avoid absorption of moisture that will cause the loss of iodine. It can be added to sausages, cheese etc (Gutekunst and Scriba, 1989). Also eggs, wine and animal foods should be added to the human diet (Carpenter, 2005). Egg yolks get the iodine from the addition of it in chicken feed (L Lee et al, 2015). Iodine can enter in the milk by the use of iodophores before and after milking. These disinfectants contain minimum of 1% of iodine which is absorbed through the skin and enters into the milk (Pearce et al, 2004). It can be found in milk due to the addition in food of the animals for the prevention of hoof rot and the decreased fertility rate in cows (L Lee et al, 2015). In addition, the consumption of iodinated bread by using iodate bread conditioner can help with the consumption of iodine (Pearce et al, 2004). This method is highly used in the United Kingdom while in Italy they use iodized water (Andersson et al, 2007).

In 1993, only five countries were facing the problem of iodine deficiency in Europe. However, over the past five to six years there is an impressive progress and this progress has to be sustained. This depends on a political commitment of the public health authorities and the decisions taken by the government, on the monitoring and evaluation system, the cooperation between the members taking part in the control of iodine deficiency and public education. Public support and training on iodine deficiency have to be retained, reinforced and initiated especially in countries where iodine deficiency is a major problem and it couldn’t be reduced despite the efforts done. The main partners involved are the public, national health authorities and the salt and food industry.

Challenges for the Member states of the European Union include: a) Programs for the prevention and control of iodine deficiency in countries with mild iodine deficiency b) public education so that the consumers can ask for iodized salts c) Increase the supplementation during pregnancy and lactation d) Surveillance programs including the information on the consumption of salt and the iodized salt in the diet e) Provide information on the function of thyroid gland f) Improvement of information on the consumption of iodine rich foods.

In some countries there is a decreasing intake of salt for the prevention of hypertension and cardiovascular diseases (Andersson et al, 2017). In addition, there have also been campaigns to reduce egg consumption to control cholesterol and blood pressure. (L Lee et al, 2015).Therefore complementary measures should be carried out to increase iodine intake (Andersson et al, 2007).

Nowadays, there is a cultivation of high-yielding cultivars and these genotypes are characterized by the low content of minerals especially iodine and selenium. For this reason, there is an introduction of plant biofortification by biotechnological or agrotechnical approaches for the improvement of accumulation of minerals in the fodder.

Another important subject is the execution of the “Second Green Revolution”, whose goal is the improvement of crop yield and to increase the concentration of minerals from soils to the food chain. This is an agro technical method of plant biofortification and is a low-cost approach for the prevention of mineral deficiency (Smolen et al, 2016).

**8. Adverse effects of excessive iodine intake.**

Adverse effects due to the increase intake of iodine are minor and are not as often as diseases caused by iodine deficiency. Enlargement of thyroid gland- goiter and subclinical hypothyroidism can occur due to the iodine enhancement of thyroid autoimmunity and reversible inhibition of thyroid function by excess iodine. Additionally, iodine induced hyperthyroidism can be a possible side effect and it can be found during the iodine supplementation programs. It is mostly being diagnosed in old patients due to the loss of mechanism of autoregulation against iodine excess (Andersson et al, 2007).

Excessive iodine intake comes from natural sources such as drinking water in Japan or iodine-rich meat and milk in Iceland. Clinical signs due to iodine poisoning can be gastrointestinal irritation, nausea, vomiting, abdominal pain and diarrhea (Zimmermann, 2009).

**9. Conclusion.**

Iodine is a chemical element and is one of the most important elements for the body. It is found in mammary tissue, salivary glands, eyes, gastric mucosa and cervix. It’s most important role is the synthesis of thyroid hormones thyroxin and triiodothyronine. This helps regulate the metabolic rate, calorigenesis, growth, thermoregulation, protein synthesis and development of most organs especially the brain

Mental retardation and CNS diseases are the most important diseases prevented by iodine intake. The period of iodine supplementation is very important during pregnancy for the prevention of CNS diseases especially cretinism thus iodine intake should be presented during the first trimester. It can be given orally or intramuscularly in the form of iodized oil. Cretinism comes from a deficient mother and results in loss of hearing.

Nowadays, iodine deficiency is a big problem. More and more countries are deficient, resulting in a huge concern for both animals and humans.

In cats the most important endocrine disease is hyperthyroidism and in dogs is hypothyroidism. Other diseases include goiter formation, myxoedema, tumor formation and reduce growth and development. The age and breed plays an important role in the formation of the disease.

In European countries, salt iodization programs seem to be an effective preventative method but unfortunately, non-iodized salt is cheaper and more often used. In animal foods, iodine content depends on the brand and the type of food. In canned food the presentation of goitrogens on the internal lining of metal cans has an antithyroid effect as well as the low iodine intake from the environment and the interaction with nutrients e.g. iron.

In some European countries, the government is taking measures for the prevention of iodine deficiency such as the public support, training and education as well as surveillance programs for the provision of information on the function of thyroid gland and the consumption of iodized salt. The use of potassium iodide in bakers and the iodized water is a good preventative way.

In farm animals, there must be iodine supplementation in animal fodder so that the iodine will enter the food chain and the range of it in milk and meat will be higher.

Nowadays, there is a decrease in intake of salt in both animals and humans due to the high rate of cardiovascular diseases and hypertension. Hence, campaigns for proper information of public will help for the increase intake and reduction of endocrine diseases.

Prevention rather than treatment of iodine deficiency is easier and more economical, therefore animals should consume the correct dosage: 25-100μg iodine per day for an average size cat and 0,70 mg/kg diet for dogs.

**10. APPENDICES**

Fig. 1

Relationship between environmental chemicals, medical therapy and risk of hyperthyroidism in cats (Kass et al, 1999)

Fig. 2

Relationship between dietary constituents and risk of hyperthyroidism (Kass et al, 1999).

Fig. 3

Clinical findings in 131 Hyperthyroid cats (Peterson, 1983).

Table 1

Effects and mechanism of action of goitrogens and Selenium deficiency (Peterson M, 2012)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Mechanism** | **Effects** | **Site(s) of action** |
| **Soy isoflavones** | Inhibition of thyroid peroxidase in thyroid follicles. | Decreased synthesis of T3 and T4. | Thyroid gland |
| **Flame retardants** | Competitive binding of thyroid hormone binding protein. | Decreased thyroid hormone delivery to brain. | Bloodstream |
| **Polybrominated diphenyl ethers** | Altered transport across cell membrane. | Increased biliary elimination of thyroid hormones. | Liver |
| **Selenium deficiency** | Inhibition of deiodinase activity. | Decreased peripheral T3 synthesis. | Kidney and Liver |
| **Bisphenol-A and Polybrominated diphenyl ethers** | Thyroid receptor antagonist. | Altered binding of T3 to thyroid hormone receptor, with altered activation of thyroid-hormone-dependent gene transcription. | Brain  Pituitary gland  Peripheral tissues |
| **Pesticides** | Inhibition of TSH receptor | Decreased production of T3 and T4. | Pituitary gland |

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