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Crentisim (Review)

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B.D.S, M.Sc. Oral Medicine

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سُورَةُ يُونُسَ

هُوَ ٱلَّذِى جَعَلَ ٱلشَّمْسَ ضِيَآءً وَٱلْقَمَرَ نُورًا
وَقَدَّرَهُۥ مَنَازِلَ لِتَعْلَمُواْ عَدَدَ ٱلسِّنِينَ وَٱلْحِسَابَ
مَا خَلَقَ ٱللَّهُ ذَٰلِكَ إِلَّا بِٱلْحَقِّ يُفَصِّلُ ٱلْأَيَٰتِ
لِقَوْمٍ يَعْلَمُونَ (5)

Certification of Supervisor

I certify that this project entitled " crentisim and its oral findings " was prepared by Tuka Mohammed under my supervision at the college of dentistry/university of Baghdad in partial fulfillment of the requirements for the degree of B.D.S.

Supervisor's name: Dr.Rana Murtadha

Dedications

" First I would like to thank Allah who bestowed upon me his knowledge and made me from where I am today …

To my idol , father and mother who guided my steps and provided love, support and appreciation all the way through , without them, I would not be with you today …

To my guardian angel , my brother " Mostafa" who support me at every moment ...

To my soul mate , my husband " Qasim" who made everything easy and possible for me …

To all my friends whom I consider my sisters , who were turn any problem or difficult day into beautiful day , and they made it easy for me a lot , especially " Hawraa" and my friends at school , the university separated us , but we remained sisters …

To my supervisor , Dr, Rana who helped to complete this review …

All love, gratitude and respect to my friends, they have been a constant source of inspiration, a special thanks is offered to them..."

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List of contents

List of figures

List of tables

Introduction

The thyroid gland is the major regulator of metabolism and affects all of the bodily functions. Thyroid dysfunction is the second most common glandular disorder of the endocrine system which may rear its head in any system in the body including the mouth. The oral cavity is adversely affected by either an excess or deficiency of these hormones. Before treating a patient who has thyroid disorder, the endocrinologist needs to be familiar with the oral manifestations of thyroid dysfunctions. The patient with a thyroid dysfunction, as well as the patient taking medications for it, requires proper risk management before considering dental treatment by the dentist. Thus, communication of dentist with endocrinologist must be bidirectional, to maintain patient's oral and thyroid health.

Cretinism is characterized by severely stunted physical and mental development caused by untreated congenital thyroid hormones deficiency (Srivastav A and Maisnam I , 2012). Cretinism is always accompanied by significant cognitive dysfunction or hearing, speech, stance, gait, and growth defects (Skeaff SA. *Nutrients.* 2011). There are two types of cretinism; symptoms of both types can sometimes be seen in the same individual (Skeaff SA. and *Nutrients.* , 2011).

Proximal spasticity is present, with significantly exaggerated deep tendon reflexes in the knee, sternocleidomastoid, and biceps (Eastman and Zimmermann , 2018). The leading cause of neurological cretinism is now thought to be maternal hypothyroidism caused by iodine deficiency(Cao XY et al , 1994).

On the other hand, Myxedematous cretinism is characterized by severe growth retardation, incomplete maturation of facial features, including the naso-orbital configuration, atrophy of the mandibles, puffy features, myxedematous, thickened and dry skin, dry and decreased hair, eyelashes, and brows, and significantly delayed sexual maturation . Goiter is typically absent, and the thyroid is commonly not palpable, revealing thyroid atrophy (Srivastav and Maisnam , 2012).

The common oral findings in hypothyroidism include the characteristic macroglossia, dysgeusia, delayed eruption, poor periodontal health, altered tooth morphology and delayed wound healing . Before treating a patient who has a history of thyroid disease, the dentist should obtain the correct diagnosis and etiology for the thyroid disorder, as well as past medical complications and medical therapy (Young , 1989) .

Aim of study

This progect was designed to review systemic oral anomalies in patients with cretinisim.

Review of literature

(1-1) Thyroid gland

The thyroid gland is a butterfly-shaped organ composed of bulbous right and left lobes connected in the midline by a thin structure called the isthmus (Maitra and Mescher , 2010). Located anterior to the neck, the thyroid wraps around the anterior trachea. Directly inferior to the larynx, at the level of the C5 through T1 vertebrae (Mescher , 2010). On average, it measures 5 cm in height, 5 cm in width, and weighs 20-30 g in adults, with slightly heavier thyroids seen in women (Mescher , 2010),Figure(1).

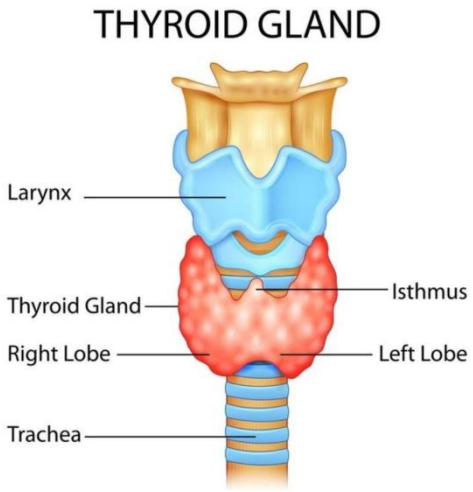


Figure no. 1 Anatomy of thyroid gland

A richly vascular structure, the thyroid receives its blood supply predominantly from two sources. The superior thyroid artery, which is the first branch of the external carotid artery, supplies the upper half of the thyroid in over 95% of people. The lower portion of the thyroid is most commonly supplied by the inferior thyroid artery, branching from the thyrocervical trunk, itself a branch of the subclavian artery; in a subset of the population, the inferior thyroid artery may be absent or duplicated (Ozgüner et al. , 2014).

The thyroid has extensive lymphatic drainage involving multiple levels of lymp nodes, including but not limited to the prelaryngeal (or Delphian), pretracheal, paratracheal, retropharyngeal, retroesophageal, and internal jugular lymph nodes. This becomes very important in the staging of thyroid carcinoma, during which careful lymph node dissection may be necessary in the search for metastases (Rosai and Tallini 2011)

1-2 Physiology of thyroid gland

Normal Physiology of thyroid gland , In order to discuss hyper- and hypothyroidism and their sequelae, one must first recall the normal physiology of the thyroid gland. The primary function of thyroid follicular cells is the synthesis of thyroid hormones, of which there are predominantly two: tetraiodothyronine (T4), more commonly known as thyroxine, and triiodothyronine (T3) (Mescher , 2010). These hormones are extremely important for a significant variety of functions throughout the body, including energy metabolism, body temperature regulation, growth, bone production, and central nervous system maturation and are essential for proper growth and brain development in infants (Maitra and Mescher , 2010). Thyroid hormone production and release is stimulated through the hypothalamic-pituitary axis. Thyrotropin-releasing hormone (TRH) from the hypothalamus causes the anterior pituitary to release thyrotropin, also called thyroid-stimulating hormone (TSH) (Mescher and Costanzo , 2010). In response to TSH, thyroid follicular cells produce thyroglobulin, an inactive protein, which is then released from the apical surface into the follicle as colloid (Costanzo , 2010). Sodium-iodide cotransporters on the basal surface of follicular cells take up iodide from the bloodstream, which is then released via transport protein, pendrin, into the follicle and oxidized by thyroid peroxidase into iodine (Mescher , 2010). Next, tyrosine residues on thyroglobulin are iodinated and then conjugated via oxidative coupling, forming T3 and T4 (Mescher , 2010). Iodinated thyroglobulin is taken back into the follicular cell, where lysosomal protease degradation releases the T3 and T4 to exit into capillaries. Thyroid hormones travel in the bloodstream bound predominantly to thyroxine-binding protein (Costanzo , 2010). T4 is significantly more abundant, making up 90% of the total thyroid hormone; however, T3 is two to ten times more bioactive (Mescher and Costanzo , 2010). To combat this problem, the target tissues contain 5′- iodinase, which can convert T4 into T3 (Costanzo , 2010). The activity of thyroid hormone is very broad, as it can act by essentially three main mechanisms: 1) directly at the cellular level, 2) via the sympathetic nervous system, and 3) through changing metabolism and affecting the circulation (Polikar et al. , 1993). Thyroid hormone increases basal metabolic rate , body temperature, gluconeogenesis, lipolysis, proteolysis, and glucose absorption. It increases stroke volume and heart rate, leading to increased cardiac output. In the young, it promotes growth and leads to bone maturation and fusion of growth plates. It is essential for central nervous system (CNS) maturation during fetal development (Costanzo , 2010).

This series of biochemical events leading to thyroid hormone formation is controlled by a negative feedback loop whereby increased levels of thyroid hormone, especially T3, inhibit release of TSH from the anterior pituitary (Costanzo , 2010). The opposing forces of TRH and T3 allow for maintenance of a relatively steady thyroid state in the normal individual (Costanzo , 2010).

However, when derangements occur within this delicate system, serious and potentially fatal conditions may result (Zhang et al. , 2014),Figure(2-3)

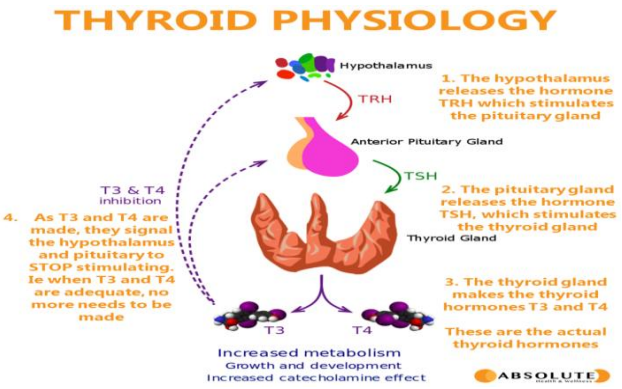


Figure no. 2

physiology of thyroid gland

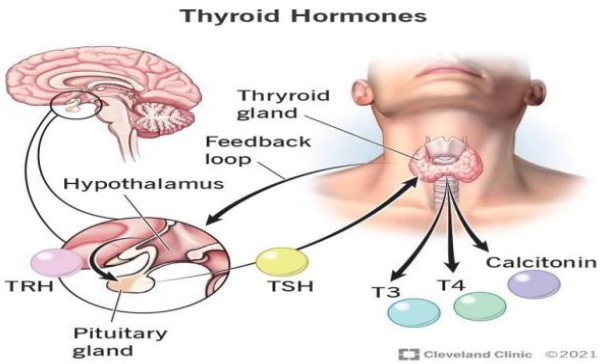


Figure no. 3

physiology of thyroid gland (

1-3 Hyper- and hypothyroidism

Hyper- and hypothyroidism are two of the most common disorders of the endocrine system worldwide (Costanzo , 2010). Approximately 4-5% of the population of the United States are affected, and the number is even higher in iodine-deficient countries (Costanzo, 2010). Most importantly, both symptomatic and asymptomatic versions of these two conditions are associated with increased mortality – in particular, due to cardiovascular disease (Wei et al. , 2013) .

1-4 Cretinism

Cretinism is an irreversible brain damage, irreversible mental retardation and severely stunted physical growth in an infant or child due to severe iodine deficiency during pregnancy caused by inadequate thyroid hormone production (congenital hypothyroidism)(Srivastav et al. , 2012). Cretinism is due to dietary iodine deficiency and can be prevented by correction of iodine deficiency before pregnancy. Cretinism is the most serious iodine deficiency disorder and occurs when a pregnant women is severely iodine deficient. The medical definition of cretinism involves three features:

(1) an association with endemic goiter (i.e. prevalence of goiter > 5 %) and severe iodine deficiency .

(2) clinical symptoms which includes some form of mental deficiency and/or defects in hearing, speech, stance, gait, hypothyroidism, and stunted growth .

(3) when iodine deficiency is corrected in the area cretinism is no longer observed (Health Jade Team , 2020).

Iodine deficiency is now recognized by the World Health Organization (WHO) as the most common preventable cause of brain damage with in excess of 2 billion at risk from 130 countries. In 1990 it was estimated that among the 1572 million people in the world exposed to iodine deficiency (28.9 % of the then world population), 11.2 million were affected by overt cretinism, the most extreme form of mental retardation due to iodine deficiency and that another 43 million people were affected by some degree of itellectual impairment . Thus, iodine deficiency was a leading global cause of preventable mental impairment (Health Jade Team , 2020).

Prenatal iodine deficiency, and the resulting fetal hypothyroidism that caused cretinism, vanished from the United States and Europe in the wake of iodization campaigns . In the United States, iodine status has remained generally adequate in since the 1940s although studies have shown that urinary iodine levels dropped by about half between the early 1970s and the early 1990s, and most recently mild iodine deficiency has re-emerged in pregnant women. Iodine deficiency remains a major issue in other parts of the world, including parts of Europe, Africa and Asia (Health Jade Team , 2020).

Congenital hypothyroidism can be endemic, genetic, or sporadic.

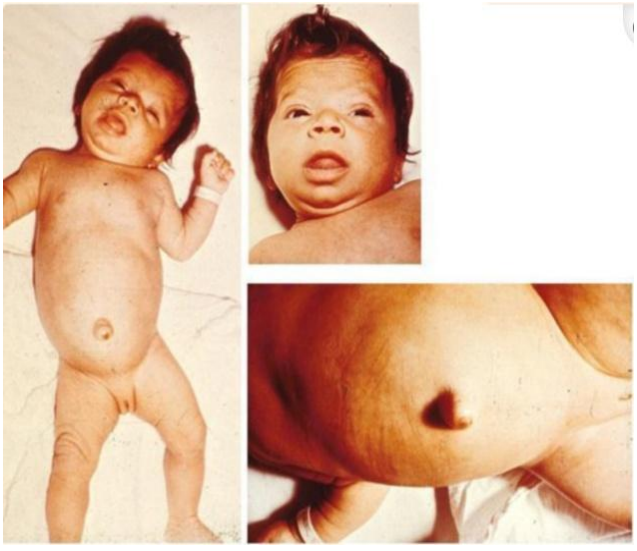
Endemic cretinism was especially common in areas of southern Europe around the Alps, Bangladesh, China, and Nepal. Endemic cretinism is now included in the spectrum of the effects of iodine deficiency in a population termed the ‘iodine deficiency disorders’, which also includes a wide range of lesser degrees of cognitive defect that can be prevented by the correction of iodine deficiency. Sporadic and genetic cretinism results from abnormal development, or function of the fetal thyroid gland (Chen ZP et. , 2010)

Cretinism has been almost completely eliminated in developed countries by early diagnosis by newborn screening schemes and iodine supplementation programs. In 2001, the World Health Organization (WHO), United Nations Children's Fund (UNICEF) and International Council for Control of Iodine Deficiency Disorders (ICCIDD) developed a system for classifying iodine deficiency based upon the median urinary iodine concentration in a population (fortification of food-grade salt with iodine for the prevention and control of iodine deficiency disorders 2014).

1-4-1 Symptoms of cretinism

Symptoms of Congenital Hypothyroidism , Early clinical manifestations of CH include hoarse cry, macroglossia, large fontanels, facial puffiness, lethargy, hypothermia, bradycardia, umbilical hernia, protuberant abdomen, feeding difficulties, hypotonia, constipation, and prolonged jaundice. Additional clinical signs include generalized myxedema, poor growth, delayed deep tendon reflexes, developmental delay, and mental retardation if left untreated or under treated.CH impacts the child's cognitive stages and neurological implications. (Grant and Smith , 1992).

The duration of fetal TH deficiency affects these outcomes differently (Prezioso and Giannini , 2018). The availability of maternal TH protects early brain development with CH, mainly through D2 (deiodinases)-mediated conversion of maternal FT4 (Prezioso and Giannini , 2018). As a result, regions of the brain that have just begun to develop, such as temporal and contextual memory, speech, hearing sorting, recognition, and executive handling, are impaired in CH (Prezioso and Giannini , 2018). When TH is insufficient in the first gestation, visual memory, gross motor development, sensory processing, and event imagination appear to be affected, comparable to maternal insufficiency (Prezioso and Giannini , 2018),Figure(4).



Picture no. 3 Infant with congenital hypothyroidism

1-4-2 Oral manifestations of cretinism

Oral findings of cretinism or congenital hypothyroidism include.(Vincent and Tavella , 2019).

1- Stunted growth.

2- Poor feeding.

3- Thickened facial features .

4- Abnormal bone growth.

5- Low muscle tone.

6- Unusually large tongue (macroglssia).

7- Swelling of the skin (myxedema).

8- Swelling in the neck from an enlarged thyroid gland (goiter).

1-4-3 Types of cretinism

There are two main types of cretinism (Chen and Hetzel , 2009)

1- Neurological cretinism is characterized by mental retardation, deaf mutism, squint, spastic diplegia, and disorders of stance and gait while.

2- Myxoedematous or hypothyroid cretinism is less common and characterized by mental retardation (although less severe than in neurological cretinism), dwarfism, and hypothyroidism with associated physical symptoms (e.g., coarse and dry skin, husky voice, delayed sexual maturation)(Chen and Hetzel , 2009).

Some countries and regions have a higher prevalence of one type of cretinism than the other, and sometimes the symptoms of both types of cretinism can manifest in the same individual. A study of 112 cretins (neurological, myxoedematous, and mixed) living in Thailand reported that their mean IQ score was 30.8 ±8.8 .In addition to the presence of cretins in a community, Chen and Hetzel state that mild mental retardation (IQ 50–69) is found in 5–15 % of children living in areas of endemic cretinism; these children are sometimes referred to as ‘sub-cretins ’(Chen and Hetzel , 2009) .

Both types of cretinism are due to dietary iodine deficiency and can be prevented by correction of iodine deficiency before pregnancy (Chen and Hetzel , 2009) .

1-4-5 Causes of cretinism

Cretinism causes, in newborn is due to severe prenatal iodine deficiency during pregnancy caused by inadequate thyroid hormone production (congenital hypothyroidism or fetal hypothyroidism). . (Chen and Hetzel , 2009) .

Congenital hypothyroidism can be endemic, genetic, or sporadic. Endemic cretinism is a developmental disorder that occurs in regions of severe endemic goiter. Both parents of an endemic cretin are usually goitrous, endemic cretins often have deaf-mutism, spasticity, motor dysfunction, and abnormalities in the basal ganglia demonstrable by magnetic resonance imaging. (Chen and Hetzel , 2009) .

Other factors such as the presence of goitrogens in the diet, thyroid immunity, and interactions with other trace elements such as selenium have also been postulated to have a role in the development of cretinism (Zimmermann , 2008) .

Nonetheless, the lack of iodine in the diets of pregnant women in the first trimester appears to be a common factor in both forms of cretinism, suggesting that maternal hypothyroidism is responsible for irreversible damage to the foetal brain. In the landmark trial of 165,000 people living in an area of Papua New Guinea with severe iodine deficiency and endemic cretinism families were allocated to iodine (iodised oil) or placebo (saline) and subsequent follow-up studies of the original cohort found that an injection of iodised oil before conception or in early pregnancy reduced the incidence of cretinism and improved the motor and cognitive functions of children compared with placebo treatment (Pharoah et al. , 1971)

Another study was undertaken in 1990 in a remote province in China with endemic cretinism . The effect of iodised oil given during pregnancy and to children up to 2 years of age on neurological outcomes was investigated by comparing treated children with untreated children at two years, and again when treated children were school-aged (O'Donnell et al. , 2002). Children of mothers given iodine earlier in pregnancy had improved cognitive outcomes compared to mothers given iodine later in pregnancy and to children treated after birth.(N Engl and Med , 1994) .

Iodine requirements in pregnancy ; Iodine turnover, thyroidal radioiodine uptake, and balance studies suggest that the average daily requirement for iodine in nonpregnant women is 91–96 μg/d (Washington , 2001). The US Estimated Average Requirement (EAR) for iodine for nonpregnant, nonlactating women aged ≥14 years is 95 μg/day, and the Recommended Dietary Allowance (RDA) is 150 μg/day (Washington , 2001). This agrees with the World Health Organization (WHO), United Nations Children's Fund (UNICEF), and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) Recommended Nutrient Intake for iodine of 150 μg/d for nonpregnant women (Geneva , 2007).

The iodine requirement during pregnancy (Glinoer , 2004) is sharply elevated

1) because of an increase by ≈50% in maternal thyroxine (T4) production to maintain maternal euthyroidism and to transfer thyroid hormone to the fetus

2) because iodine needs to be transferred to the fetus for fetal thyroid hormone production, particularly in later gestation

3) because of a probable increase in renal iodine clearance (Glinoer , 2004) .

The US EAR is 160 μg/day for pregnancy in women aged ≥14 years, and the Recommended Dietary Allowance, set at 140% of the EAR rounded to the nearest 10 μg, is 220 μg/d (Washington , 2001). Recently, the WHO/UNICEF/ICCIDD increased the Recommended Nutrient Intake for iodine during pregnancy from 200 to 250 μg/day (Geneva , 2007), but emphasized the need for more data on the level of iodine intake [and the corresponding urinary iodine (UI) concentration] that ensures maternal and newborn euthyroidism.

1-4-6 Diagnosis of cretinisim

Cretinism diagnosed by ; Maternal urinary iodine concentration

The median urinary iodine concentration is recommended by the World Health Organization (WHO) 17 for assessing iodine intake in populations of nonpregnant and pregnant women. Daily iodine intake can be extrapolated from the urinary iodine concentration assuming 24-hour urine volumes and iodine bioavailability of 92% (Washington , 2001) ; the recommended daily iodine intake during pregnancy of 220–250 μg (Geneva , 2007) would correspond to a median urinary iodine concentration of 135–155 μg/L during pregnancy. Pregnancy may occur in adolescence, particularly in developing countries; during pregnancy this extrapolation of iodine intake from the urinary iodine concentration may be less valid because of an increase in renal iodine clearance (Glinoer , 2004).

If renal iodine clearance increases in pregnancy, the daily iodine intake extrapolated from the urinary iodine concentration in pregnancy would be lower than that in nonpregnancy. (Washington , 2001) .

More reference data on urinary iodine concentrations in chronically iodine-sufficient pregnant women, including trimester-specific values, would be valuable. (Washington , 2001) .

The WHO currently recommends that a median urinary iodine concentration in a population of pregnant women of 150–249 μg/L indicates adequate iodine intake (Table 3). However, this population indicator should not be used for the purposes of individual diagnosis and treatment. (Washington , 2001).

Table 1. Epidemiologic criteria for assessing iodine nutrition in a population of pregnant women based on median urinary iodine concentrations (Washington , 2001) .

Median urinary iodine	Iodine intake
<150 µg/L	**Insufficient**
150–249 µg/L	**Adequate**
250–499 µg/L	**More than adequate**
≥500 µg/L	**Excessive**

1-4-7 Neonatal screening for cretinism

The aim of neonatal screening is the earliest identification of any form of congenital hypothyroidism, but particularly those patients with severe hypothyroidism in whom disability is greatest if not treated (Health Jade Team , 2020).

The identification of central congenital hypothyroidism by screening programs is under debate. Two screening strategies for the detection of congenital hypothyroidism have evolved (Health Jade Team , 2020).

In the primary T4/backup TSH method, still favored in much of North America and the Netherlands, T4 is measured initially while TSH is checked on the same blood spot in those specimens in which the T4 concentration is low. In the primary TSH approach, favored in most parts of Europe and Japan, blood TSH is measured initially (Health Jade Team , 2020).

A primary T4/backup TSH program will detect overt primary hypothyroidism, secondary or tertiary hypothyroidism, babies with a low serum T4 level but delayed rise in the TSH concentration, TBG deficiency and hypothyroxinemia; this approach may, however, miss subclinical hypothyroidism (Health Jade Team , 2020).

A primary TSH strategy, on the other hand, will detect both overt and subclinical hypothyroidism, but will miss secondary or tertiary hypothyroidism, a delayed TSH rise, TBG deficiency and hypothyroxinemia. There are fewer false positives with a primary TSH strategy. Both programs will miss the rare infant whose T4 level on initial screening is normal but who later develops low T4 and elevated TSH concentrations. This pattern has been termed “atypical” congenital hypothyroidism or “delayed TSH” and is observed most commonly in premature babies with transient hypothyroidism or infants with less severe forms of permanent disease (Health Jade Team , 2020).

According to the European Society for Pediatric Endocrinology (ESPE) guidelines, the most sensitive test for detecting primary congenital hypothyroidism is the determination of TSH concentration that detects primary congenital hypothyroidism more effectively than primary T4 screening Primary T4 screening with confirmatory TSH testing can detect some cases of central congenital hypothyroidism, but some cases of mild congenital hypothyroidism can be missed, depending on the cutoff T4 value used (Health Jade Team , 2020).

Physicians caring for infants need to appreciate that there is always the possibility for human error in failing to identify affected infants, whichever screening program is utilized. This can occur due to poor communication, lack of receipt of requested specimens, or the failure to test an infant who is transferred between hospitals during the neonatal period. Therefore, if the diagnosis of hypothyroidism is suspected clinically, the infant should always be tested. Adult normative values, provided by many general hospital laboratories, differ from those in the newborn period and should never be employed (Health Jade Team , 2020).

Congenital hypothyroidism is defined on the basis of serum FT4 levels as severe when FT4 is <5 pmol/l, moderate when FT4 is 5 to 10 pmol/l, and mild when FT4 is 10 to 15 pmol/l, respectively. Determination of serum thyroglobulin (Tg) is useful, if below the detection threshold, to suggest athyreosis or a complete thyroglobulin synthesis defect. Measurement of thyroglobulin is most helpful when a defect in thyroglobulin synthesis or secretion is being considered. In the latter condition the serum thyroglobulin concentration is low or undetectable despite the presence of a normal or enlarged, eutopic thyroid gland. Serum thyroglobulin concentration also reflects the amount of thyroid tissue present and the degree of stimulation. For example, thyroglobulin is undetectable in most

patients with thyroid agenesis, intermediate in babies with an ectopic thyroid gland, and may be elevated in patients with abnormalities of thyroid hormonogenesis not involving thyroglobulin synthesis and secretion. Considerable overlap exists, and so, the thyroglobulin value needs to be considered in association with the findings on imaging. In patients with inactivating mutations of the TSH receptor discordance between findings on thyroid imaging and the serum thyroglobulin concentration has been described in some but not all studies(Health Jade Team , 2020).

Imaging studies are helpful to determine the specific etiology of congenital hypothyroidism. Both scintigraphy and ultrasound (US) should be considered in neonates with high TSH concentrations. Ideally, the association of US and scintigraphy gives the best information in a child with primary hypothyroidism. Scintigraphy shows the presence/absence (athyreosis), position (ectopic gland, in any point from the foramen caecum at the base of the tongue to the anterior mediastinum) and rough anatomic structure of the thyroid gland. US, is a useful tool in defining size and morphology of a eutopic thyroid gland, however, US alone is less effective in detecting ectopic glands. Color Doppler US improves the effectiveness of US. It is important to remember that an attempt to obtain imaging in a newborn should never delay the initiation of treatment(Health Jade Team , 2020).

Combining scintigraphy and thyroid ultrasound improves diagnostic accuracy and helps to address further investigations, including molecular genetic studies. Infants found to have a normal sized gland in situ in the absence of a clear diagnosis should undergo further reassessment of the thyroid axis and imaging at a later age(Health Jade Team , 2020).

1-4-8 Prevention of cretinism

Cretinism prevention ; For nearly all countries, the primary strategy for sustainable elimination of iodine deficiency in pregnancy remains universal salt iodization (Geneva 2007). However, implementation of universal salt iodization is not always feasible, which may result in insufficient access to iodized salt for women of childbearing age and pregnant women. Iodine supplementation of these groups should be considered (Geneva 2007) .

An adequate iodine supply should continue after parturition, because the iodine requirement of a women who is fully breastfeeding her infant is likely even higher than that during pregnancy (Health Jade Team , 2020).

In countries or areas where <90% of households are using iodized salt and the median urinary iodine concentration in schoolchildren is <100 μg/L, the recommendations for iodine supplementation in pregnancy and infancy are shown in Table 2.

Table 2. Recommendations for iodine supplementation in pregnancy and infancy in areas where <90% of the households are using iodized salt and the median urinary iodine concentration in schoolchildren is <100 μg/L.(Health Jade Team , 2020).

Women of childbearing age	**Single annual oral dose of 400 mg I as iodized oil** **Daily oral dose of iodine as potassium iodide to meet the Recommended Nutrient Intake of 150 μg I/d**
Pregnant or lactating women	**Single annual oral dose of 400 mg I as iodized oil**
	Daily oral dose of iodine as potassium iodide to meet the new Recommended Nutrient Intake of 250 μg I/d **Iodine supplements should not be given to women who already received iodized oil during current pregnancy or up to 3 mo before current pregnancy started**

1-4-9 Treatment of cretinism

Cretinism treatment ; Timing of normalization of thyroid hormones is critical for brain development and therefore replacement therapy with L-thyroxine (L-T4) should be begun as soon as the diagnosis of congenital hypothyroidism is confirmed. The aims of therapy are to normalize the T4 as soon as possible, to avoid hyperthyroidism where possible, and to promote normal growth and development. The current recommendations for the initiation of treatment are thyroxine 10 to 15 μg/kg/day, crushed on a spoon and mixed in milk or water, but not put in the bottle so as to ensure full dose delivery. The tablets are sweet, and the taste is not unpleasant. The highest dose is indicated in infants with severe

disease, and the lower dose in those with a mild to moderate congenital hypothyroidism. L-thyroxine tablets can be crushed and given via a small spoon, with suspension, if necessary in a few milliliters of water or breast milk or formula or juice, but care should be taken that all of the medicine has been swallowed. Thyroid hormone should not be given with substances that interfere with its absorption, such as iron, calcium, soy, or fiber. Drugs such as antacids (aluminum hydroxide) or infantile colic drops (simethicone) can interfere with L-thyroxine absorption . Many babies will swallow the pills whole or will chew the tablets with their gums even before they have teeth. Reliable liquid preparations are not available commercially in the US, although they have been used successfully in Europe(Segni , 2000) .

When an initial dosage of 10-15 mcg/kg is used, the T4 will normalize in most infants within 1 week and the TSH will normalize within 1-month (Segni M , 2000). Subsequent adjustments in the dosage of medication are made according to the results of thyroid function tests and the clinical picture. Often small increments or decrements of L-thyroxine (12.5 mcg) are needed. This can be accomplished by 1/2 tablet changes, by giving an alternating dosage on subsequent days, or by giving an extra tablet once a week (Segni , 2000).

1-4-10 Dental Management

1. Patients with long standing hypothyroidism may have increased subcutaneous mucopolysaccharides due to decrease in the degradation of these substances. The presence of excess subcutaneous mucopolysaccharides may decrease the ability of small blood vessels to constrict when cut and may result in increased bleeding from infiltrated tissues, including mucosa and skin. Local pressure for an extended time will probably control the bleeding from the small vessels adequately.(Silverton , 2003) .

2. Susceptibility to infection - Patient with hypothyroidism may have delayed wound healing due to decreased metabolic activity in fibroblasts . Delayed wound healing may be associated with an increased risk for infection because of the longer exposure of the unhealed tissue to pathogenic organisms . (Silverton , 2003) .

3. Patients who have hypothyroidism are susceptible to cardiovascular disease from arteriosclerosis and elevated LDL. Before treating such patients, consult with their primary care providers who can provide information on their cardiovascular statuses. Patients who have atrial fibrillation can be on anticoagulation therapy and might require antibiotic prophylaxis before invasive procedures**,** depending

on the severity of the arrhythmia. If valvular pathology is present, the need for antibiotic prophylaxis must be assessed (Muzyka , 1999) **.**

4. Drug actions and interactions - Patients who have hypothyroidism are sensitive to central nervous system depressants and barbiturates, so these medications should be used sparingly (Malamed and Louis , 2006).

5. It has been found that recent exposure to a surgical antiseptic that includes iodine (such as Povidone) can increase the risk of thyroiditis or hypothyroidism . Patients with underlying thyroid antibodies and a tendency toward autoimmunity appear to be at more risk (Sherman and Lasseter , 1996).

6. Drug interactions of l-thyroxine include increased metabolism due to phenytoin, rifampicin and carbamazepine, as well as impaired absorption with iron sulfate, sucralfate and aluminum hydroxide. When l-thyroxine is used, it increases the effects of warfarin sodium and, because of its gluconeogenic effects; the use of oral hypoglycemic agents must be increased. Concomitant use of tricyclic antidepressants elevates l-thyroxine levels. Appropriate coagulation tests should be available when the patient is taking an oral anticoagulant and thyroid hormone replacement therapy (Carlos et al. , 2010) .

(2) Conclusion

1. Crentisim is a common endocrine disease that may be associated with severe congenital anomalies.

2. Early identification and treatment are essential to avoid long-term negative consequences and enhance better results.

3. Therapy with L-T4 must begin soon, particularly within the first two weeks after birth, and thyroid performance should be established and sustained adequately.

4. The life-long effects on growth and development and possible long-term cardiovascular and psychosocial health are considerable, emphasizing the importance of future pediatric research investigating .

5. Dental treatment modifications may be necessary for dental patients who are under medical management and follow-up for a thyroid condition even if there are no comorbid conditions.

6. Stress reduction, awareness of drug side effects or interactions, and vigilance for appearance of signs or symptoms of hormone toxicity are among the responsibilities of the oral health care provider.

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