Congenital Hypothyroidism

Congenital hypothyroidism is present at, or before, birth. Children who develop primary hypothyroidism when aged 2 years or older have poor growth and slow mentation but generally do not exhibit the profound and incompletely reversible neurologic abnormalities observed in untreated congenital hypothyroidism.

Congenital hypothyroidism is inadequate thyroid hormone production in newborn infants. This can occur because of an anatomic defect in the gland, an inborn error of thyroid metabolism, or iodine deficiency.

Despite its efforts, the World Health Organization (WHO) has not been able to completely eliminate iodine deficiency throughout the world. As a result, endemic goiter and cretinism are still observed in some areas, such as regions of Bangladesh, Chad, China, Indonesia, Nepal, Peru, and Zaire.

The thyroid gland develops between 4 and 10 weeks' gestation. Errors in the formation or migration of thyroid tissue can result in thyroid aplasia, dysplasia, or ectopy. By 10-11 weeks' gestation, the fetal thyroid is capable of producing thyroid hormone. By 18-20 weeks' gestation, blood levels of T4 have reached term levels. The fetal pituitary-thyroid axis is believed to function independently of the maternal pituitary-thyroid axis.

The thyroid gland uses tyrosine and iodine to manufacture T4 and triiodothyronine (T3). In most situations, T4 is the primary hormone produced by and released from the thyroid gland.

Inborn errors of thyroid metabolism can result in congenital hypothyroidism in children with anatomically normal thyroid glands.

T4 is the primary thyronine produced by the thyroid gland. Only 10-40% of circulating T3 is released from the thyroid gland. The remainder is produced by monodeiodination of T4 in peripheral tissues. T3 is the primary mediator of the biologic effects of thyroid hormone and does so by interacting with a specific nuclear receptor. Receptor abnormalities can result in thyroid hormone resistance.

The contributions of maternal thyroid hormone levels to the fetus are thought to be minimal, but maternal thyroid disease can have a substantial influence on fetal and neonatal thyroid function. Immunoglobulin G (IgG) autoantibodies, as observed in

autoimmune thyroiditis, can cross the placenta and inhibit thyroid function. Thioamides used to treat maternal hyperthyroidism can also block fetal thyroid hormone synthesis. Most of these effects are transient. Radioactive iodine administered to a pregnant woman can ablate the fetus's thyroid gland permanently.

The importance of thyroid hormone to brain growth and development is demonstrated by comparing treated and untreated children with congenital hypothyroidism. Thyroid hormone is necessary for normal brain growth and myelination and for normal neuronal connections. The most critical period for the effect of thyroid hormone on brain development is the first few months of life.

In areas of iodine deficiency, the prevalence of goiter is reported to range from 5-15% of the population, with a lower incidence of hypothyroidism.

Data from most countries with well-established newborn screening programs indicate an incidence of congenital hypothyroidism of about 1 per 3000-4000.[2,3] Some of the highest incidences (1 in 1400 to 1 in 2000) have been reported from various locations in the Middle East. The incidence of congenital hypothyroidism in Bangladesh is yet to be established. But there is strong suspicion of having a large number babies with congenital hypothyroidism. The incidence of congenital hypothyroidism is approximately 1 per 4000 births in USA.

Congenital hypothyroidism is observed in all populations. The racial differences observed in endemic cretinism are probably related more to geographic location and socioeconomic status than to any particular racial predilection.

Profound mental retardation is the most serious effect of untreated congenital hypothyroidism. Severe impairment of linear growth and bone maturation also occurs. Affected infants whose treatment is delayed can have neurologic problems such as spasticity and gait abnormalities, dysarthria or mutism, and autistic behavior.

Two clinical forms of endemic cretinism are described, with considerable overlap between them. The neurologic form is characterized by mental retardation, spasticity, ataxia, and defects in speech and hearing to the point of deaf-mutism. Thyroid function and stature are usually normal. Iodine deficiency in early fetal life is thought to be the

cause. In the myxedematous form, marked growth delay, myxedema (a doughy edema of the skin and subcutaneous tissue from proteinaceous fluid), and mental retardation without other neurologic features are present. Considerable geographic variation among the predominant forms and findings is noted. Most studies of congenital hypothyroidism suggest a female-to-male ratio of a 2:1.

In regions of iodide deficiency and a known prevalence of endemic cretinism, the diagnosis may be straightforward. Infants with congenital hypothyroidism are usually born at term or after term.

Symptoms and signs include the following: Decreased activity, Large anterior fontanelle, Poor feeding and weight gain, Small stature or poor growth, Jaundice, Decreased stooling or constipation, Hypotonia, Hoarse cry.

Often, they are described as "good babies" because they rarely cry and sleep most of the time.

Family history should be carefully reviewed for information about similarly affected infants or family members with unexplained mental retardation.

Maternal history of a thyroid disorder and mode of treatment, whether before or during pregnancy, can occasionally provide the etiology of the infant's problem.

Congenital hypothyroidism is more common in infants with birth weights less than 2,000 g or more than 4,500g.

Infants with obvious findings of hypothyroidism (eg, macroglossia, enlarged fontanelle, hypotonia) at the time of diagnosis have intelligence quotients (IQs) 10-20 points lower than infants without such findings.

Diagnosis of primary hypothyroidism is confirmed by demonstrating decreased levels of serum thyroid hormone (total or free T4) and elevated levels of TSH.

If maternal antibody–mediated hypothyroidism is suspected, maternal or neonatal antithyroid antibodies may confirm the diagnosis.

TBG levels can be measured in infants with suspected TBG deficiency. This condition does not require treatment, but appropriate diagnosis and parental counseling can avoid later confusion and misdiagnosis.

Routine laboratory testing in patients with TBG deficiency shows a low total T4 level and a TSH level within the reference range. Free T4 and T3 levels are within the reference range.

Thyroid scanning (using technetium-99m or iodine-123)

Ultrasonography may be a reasonable alternative to scintigraphy but may fail to reveal some ectopic glands.

The mainstay in the treatment of congenital hypothyroidism is early diagnosis and thyroid hormone replacement.

Endemic cretinism can be prevented by appropriate iodine supplementation. Iodization of salt is the usual method, but cooking oil, flour, and drinking water have also been iodinated for this purpose. Long-acting intramuscular injections of iodized oil have been used in some areas.

Dietary iodide supplementation, especially in endemic areas, can prevent endemic cretinism.

Soy-based formulas may decrease the absorption of levothyroxine.

Activity should be encouraged in children with congenital hypothyroidism, because activity should be encouraged in all children.

Only levothyroxine is recommended for treatment and has been established as safe, effective, inexpensive, easily administered, and easily monitored.

Children with congenital hypothyroidism should be monitored clinically and biochemically. Clinical parameters should include linear growth, weight gain, developmental progression, and overall well-being.

Laboratory measurements of T4 (total or free T4) and TSH should be repeated 4-6 weeks after initiation of therapy, then every 1-3 months during the first year of life and every 2-4 months during the second and third years.

Dietary iodide supplementation can prevent endemic goiter and cretinism, but not sporadic congenital hypothyroidism.

Properly administered newborn screening programs have made diagnosis of infants with congenital hypothyroidism possible within the first 3 weeks of life. With early and adequate treatment, the sequelae can be eliminated in most and minimized in the rest.

Methods of prenatal diagnosis and treatment are being evaluated.

Early diagnosis and treatment of congenital hypothyroidism prevents severe mental retardation and other neurologic complications. Even with early treatment, some children demonstrate mild delays in areas such as reading comprehension and arithmetic in third grade.

Parents should be educated regarding their child's disorder, the potential problems associated with no treatment or inadequate treatment, and the benefits of early and appropriate treatment. This should include instructions on the proper administration of the medication and how and when to follow up with the physician. Because learning problems are possible, even with early diagnosis and treatment, parents should be advised when to seek psychomotor and educational evaluations and interventions. Early childhood intervention programs, if available, should be encouraged.

When inborn errors of thyroid hormone production are suspected, genetic counseling should be provided.