



## Endocrine Complications of Cystinosis

Elena Levtschenko, MD, PhD

**E**ndocrine organs are frequently affected in cystinosis, especially in patients who are not treated adequately with cysteamine.

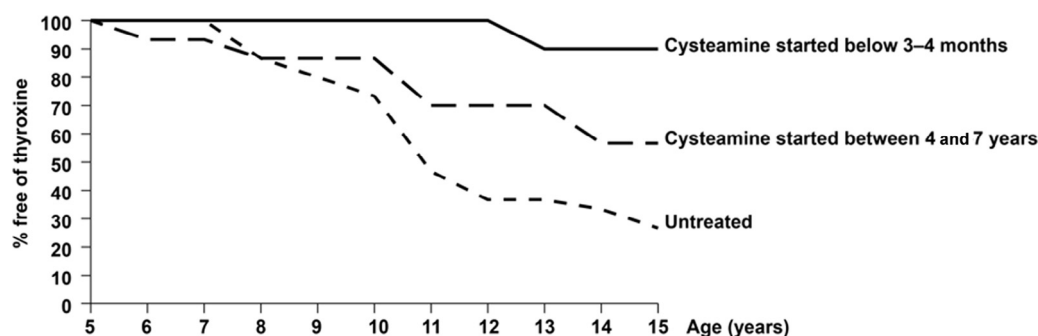
### Hypothyroidism

Thyroid dysfunction chronologically follows kidney dysfunction and develops in about 50% of untreated children by 5-10 years of age.<sup>1</sup> In 1970, Chan et al<sup>2</sup> were the first to describe primary hypothyroidism in cystinosis and performed a histologic examination of the thyroid gland showing cystine crystal accumulation and fibrosis. Biochemically, hypothyroidism usually manifests with elevated thyroid stimulating hormone (TSH), but normal T4 levels (subclinical disease), and progresses toward overt hypothyroidism over subsequent years, requiring thyroxin supplementation.<sup>3</sup> In some patients, pituitary resistance to thyroxin has been reported and is characterized by elevated TSH levels despite absence of clinical or biochemical signs of hypo- or hyperthyroidism.<sup>4</sup> In such patients, TSH fails to normalize even if serum T4 concentrations are at the upper limit of normal because of adequate thyroxin therapy.

The pathogenesis of thyroid dysfunction appears to be more complex than merely thyroid gland destruction by lysosomal cystine. In early disease, accelerated thyrocyte turnover with increased cell proliferation plus enhanced apoptosis linked to endoplasmic reticulum stress yields impaired thyroglobulin production and altered endolysosomal trafficking and iodothyroglobulin processing as has been recently demonstrated in the knockout mouse model of cystinosis.<sup>5</sup> Importantly, cysteamine treatment prevents hypothyroidism in the majority of patients with cystinosis underscoring the essential role of cystine accumulation in the development of thyroid dysfunction (Figure 1).<sup>6,7</sup>

### Diabetes Mellitus

This complication of cystinosis usually develops during adolescence or adulthood in about 5% of the patients.<sup>1</sup> However, longitudinal systematic evaluation of the endocrine pancreas by oral glucose tolerance test in post-transplant patients in the



**Figure 1.** Actuarial survival of patients with cystinosis free of thyroxin treatment according to the age at start of cysteamine treatment. Adapted from Tete et al.<sup>6</sup>

CKD Chronic kidney disease  
GH Growth hormone

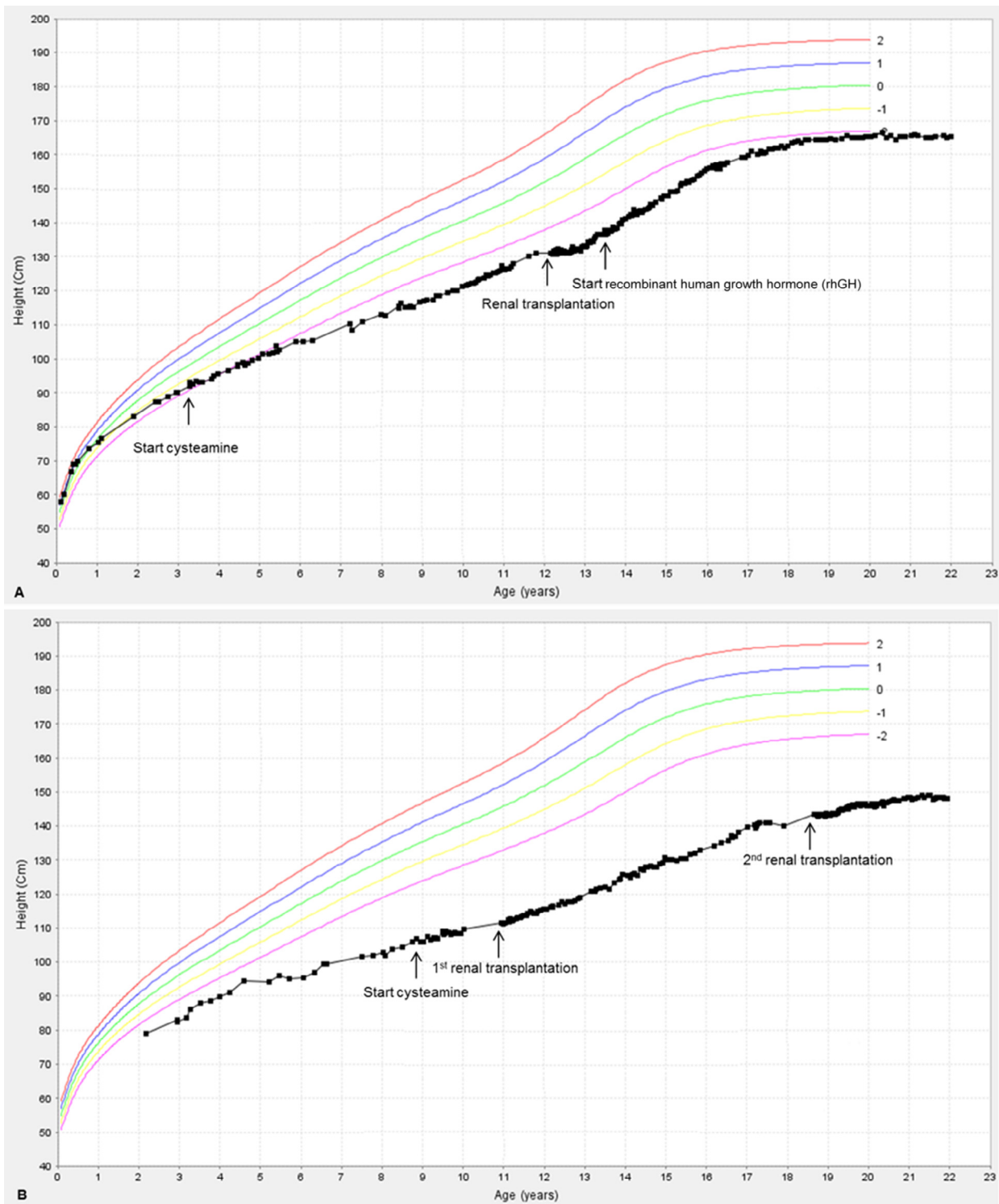
rhGH Recombinant human GH  
TSH Thyroid stimulating hormone

From the Department of Pediatric Nephrology and Development and Regeneration, University Hospitals Leuven, University of Leuven, Leuven, Belgium

Please see the author disclosures at the end of the article.

0022-3476/\$ - see front matter. © 2017 Elsevier Inc. All rights reserved.

<http://dx.doi.org/10.1016/j.jpeds.2016.12.049>



**Figure 2.** Growth curves of 2 siblings with cystinosis. **A**, Growth curve of the younger sibling. Diagnosis of cystinosis was made at the age of 5 months and confirmed by molecular analysis of the CTNS gene showing common homozygous 57 kb deletion. Note the initial normal growth after birth, with decreased growth velocity during the first months of life. A temporary improvement in longitudinal growth occurred after initiation of cysteamine therapy at the age of 3 years. Initiation of recombinant human growth hormone (rhGH) therapy after renal transplantation resulted in catch-up growth after a period of stunting; **B**, Growth curve of the older sibling, who was diagnosed at the age of 3 years and cysteamine initiated at age 9 years. Note the severe growth retardation at diagnosis, which worsened in the years thereafter. Cysteamine administration did not improve longitudinal growth. Renal transplantation did improve longitudinal growth, resulting in growth paralleling the normal growth curves, but there was no catch-up growth. Adapted from Besouw et al.<sup>17</sup>

Download English Version:

<https://daneshyari.com/en/article/5719254>

Download Persian Version:

<https://daneshyari.com/article/5719254>

[Daneshyari.com](https://daneshyari.com)