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Controversies in diagnosing and treating Growth Hormone Deficiency

Controversias en el diagnóstico y tratamiento de la deficiencia de la hormona de crecimiento

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The first reported treatment of a human with human growth hormone (GH) appeared in the *New England Journal of Medicine* in 1958. In the ensuing 66 years, GH treatment has generally proved to be quite successful, but not without its share of controversies.

Discussing the controversies related to GH would take much more time than the time we have allotted for this presentation, but here are some of them.

All treatment involving GH treatment, especially in paediatrics, should be monitored very carefully for both its efficacy and safety. I disagree with *adult height predictions*, given how incredibly inaccurate they are and how they are heavily dependent on measuring bone ages. Anyone who has looked at bone ages for more than a few years will have come to realize how imprecise these measurements are.

There have been initiatives for the *assay standardization* of GH and IGF-1. I believe harmonizing GH assays and IGF-1 assays would be extremely important, and it is still in its infancy, even though it has been discussed for some time.

If a child is growing less than would be expected for their age and bone age, *baseline evaluations* must be obtained. Low IGF-1 values overlap with abnormally low values in infants. IGFBP-3 has also been used, and if the combination of IGF-1 and IGF BP-3 are low, a *growth hormone stimulation test* (GHST) could be considered for the diagnosis of GH deficiency. There are more than 60 different agents that have been reported as stimulating GH. Unfortunately, there are no age-adjusted normal values for the responses like those we have for many other analytes in endocrinology.

Many articles on this subject have recently been published.

As to the question whether GH stimulation test should be “primed” or not, *priming* means administering testosterone or estrogen to a prepubertal child, and measuring the GH response following a standard stimulation test. We thought it would be important to ask the following question: are you looking to see what the child's response to the GHST is at this point, at this stage of his or her life? If so, perform the test without artificial “priming”; if the question is what the GH response will be when the child is going through puberty, then stimulated “primed” testing should be performed. It is more important to decide who should be tested rather than how you should be testing. Tests should certainly only be carried out when we are prepared to take action based on the result. The diagnosis of GH deficiency is indeed a clinical diagnosis. All consensus conferences on GH deficiency still include a GH stimulation test as an integral part.

Weekly or *Long Acting* GH?

Several LAGH preparations have been approved for use by the FDA in the United States in the past two years. Many other preparations are in production

worldwide. Controversies about the weekly preparation include the lack of long-term experience, unclear dose monitoring and adjustment versus IGF-1 levels, and insufficient long-term results for both efficacy and safety.

Most of the patients currently treated worldwide are patients with *idiopathic isolated GH deficiency*. We have recently made progress in the concept of evolving idiopathic isolated GH deficiency.

Growth failure with an unknown etiology, referred to by many, particularly in the United States, as *Idiopathic Short Stature*, remains a highly controversial topic. However, this category will apply to fewer children as a result of advances in molecular genetic techniques and careful longitudinal observation.

The future should see precision individualized care for children with growth disorders. Precision medicine would ideally be able to perform a genetic/molecular evaluation of a child and identify specific markers for accurate diagnosis, and then treatment could be individually tailored for that child. We are not quite there yet.