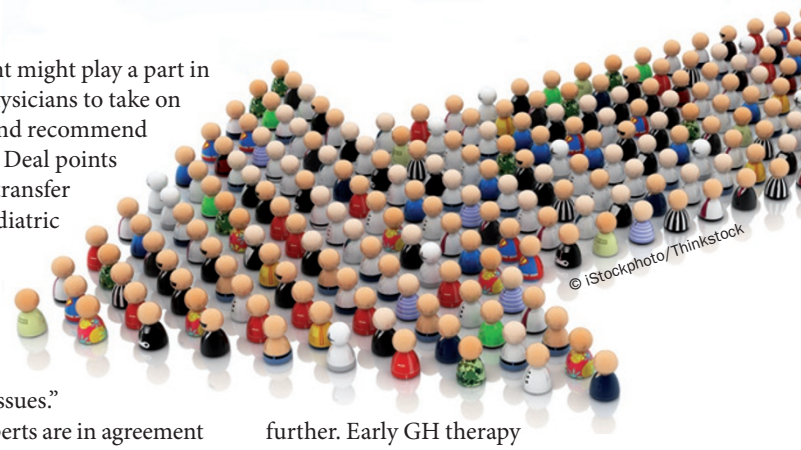
Nature Reviews Endocrinology **9**, 313 (2013); published online 23 April 2013; doi:10.1038/nrendo.2013.88

GROWTH HORMONE IN HEALTH AND DISEASE

Consensus guidelines for GH therapy in Prader–Willi syndrome—this way forward?



New recommendations for the use of recombinant human growth hormone (GH) in children and adults with Prader–Willi syndrome (PWS) highlight the overall positive benefits of GH therapy in this patient population. Moreover, the guidelines by Deal *et al.* provide an update on the follow-up of patients with PWS and incorporate new data on safety monitoring.

"The initial enthusiasm for GH therapy in patients with PWS was tempered by concerns about the impact of GH on worsening obstructive sleep apnoea and even a potential link with sudden death," recounts lead author Cheri L. Deal (CHU Sainte-Justine, University of Montreal). The heterogeneity of clinical practice in Canada (and potentially other countries) with regard to GH therapy—with some centres treating all patients with PWS, some treating about 50% of patients and some treating none—led to increasing pressure from patient support groups to provide a uniform approach to treatment.

Using a systemized approach to grading and with consideration of factors besides efficacy and safety, a consensus panel consisting of 43 international experts reviewed the current clinical evidence on GH therapy in PWS to develop a set of 15 clinical practice recommendations. Their report differs from previous publications in the strict protocol used for grading the literature (according to strength and level of evidence) and the provision of a final score for the level of recommendation.

Patients with PWS have varying degrees of cognitive impairment, can be morbidly obese if left untreated, and are in need of a wide range of health services to address all comorbidities. Unlike insulin for the treatment of type 1 diabetes mellitus, GH therapy in PWS is not a life-saving treatment, at least in the short term. Hence, physicians who deal with these patients face the dilemma of deciding whether or not to treat with GH, especially if patient consent is difficult to procure. "Societal views of extreme obesity and/or cognitive impairment might play a part in the willingness of physicians to take on patients with PWS and recommend treatment with GH," Deal points out. "Moreover, the transfer of patients from paediatric to adult care can be complex, given that many patients with PWS have severe behavioural or even psychiatric issues." Nevertheless, the experts are in agreement that impaired cognitive ability should not be a contraindication for GH therapy.

"I think it is encouraging that the authors mention that cognitive impairment should not be a barrier to treatment with GH in patients with PWS," says Dong-Kyu Jin (Sungkyunkwan University, Seoul, Korea), who is not associated with the guidelines. "A previous study showed beneficial effects of GH treatment on cognition in children with PWS, and GH treatment improves cognition in animal models. Therefore, in my opinion, this treatment effect should be emphasized."

An important addition to previous consensus recommendations is the call for rigorous documentation of favourable changes with GH therapy, including psychomotor and cognitive development, body composition, strength and exercise tolerance, and quality of life of patients and caregivers. These changes should be monitored by all individuals involved in the decision on whether to continue treatment of a patient, according to the guidelines.

The optimal age at treatment initiation remains controversial, although Deal *et al.* agree that starting GH therapy before the onset of obesity, which is often as early as 2 years of age in patients with PWS, is beneficial. "In the clinical setting, GH treatment is often initiated as soon as possible after genetic confirmation of the diagnosis of PWS," says Jin, who recommends that the importance of early initiation of GH treatment be highlighted further. Early GH therapy can increase muscle strength in the hypotonic stage, as well as improve energy expenditure and body composition.

Also novel to the guidelines by Deal *et al.* is a list of priorities for future research. Given the heterogeneous background of the expert panel, the general agreement among the participants is encouraging, not only for the individual guidelines but also for the identification of important knowledge gaps that deserve attention.

"When prescribed and monitored by experts, with appropriate teaching provided to parents and health professionals (particularly concerning the need to maintain a high index of suspicion for sleep-disordered breathing and concomitant infection), the gains of GH therapy far outweigh the risks," comments Deal. "The theme throughout the recommendations is the importance of a global treatment plan, before and during GH treatment, that must include consideration of the environment (diet and activity). It is my hope that these guidelines take GH therapy in PWS to a new level of rigour and help caregivers of these patients navigate health-care decisions."

Linda Koch

Original article Deal, C. L. *et al.* Growth Hormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader–Willi syndrome. *J. Clin. Endocrinol. Metab.* doi:10.1210/jc.2012-3888