It has been 50 years since the first family with Laron syndrome (LS, primary growth hormone (GH) insensitivity) was referred to the newly established Pediatric Endocrine Clinic at the Beilinson Hospital, Petah Tikva, Israel, a referral center now located at the Schneider Children’s Medical Center on the same campus. Since then, 64 patients have been diagnosed by the same team, investigated, and the majority followed by them, most at regular intervals, throughout childhood into adult age. This was the reason to base this book on the data accumulated from this cohort of patients forthwith called the Israeli cohort.

It was also our privilege to be the first to determine its etiopathology and the first to study the effects of insulin-like growth factor-I (IGF-I) replacement therapy in these patients. The great amount of data accumulated during half a century in the large Israeli cohort of untreated and IGF-I treated LS patients is a unique source of knowledge which we thought should be shared and presented in a united manner.

The clinical portion of this book represents a compendium of the Israeli team’s experience with LS from discovery, the struggle to define its pathogenesis, to determine the consequences if not treated by IGF-I, and the results of long-term IGF-I treatment. Reference to studies by other investigators are included when found appropriate.

During this 50 year-long journey, LS has proven to be a unique model to learn the effects of congenital IGF-I deficiency, the pharmacology of IGF-I, and the GH-IGF-I interrelationships. The fact that LS is a condition in which the action of pituitary GH is excluded permits the comparison between isolated GH deficiency and IGF-I deficiency as well as the comparison between the responses to IGF-I and hGH replacement therapies. To enable the comparison of findings in the same patient, we have identified certain patients by their initials.

In an attempt to generate an animal model of LS (GH resistance/insensitivity and IGF-I deficiency), the GH receptor gene disrupted the “knock-out” mouse (or Laron Mouse) was produced in the Kopchick laboratory in 1991. Experiments that could not be carried out in humans could now be advanced in this GH insensitive mouse. We are happy to review the results of studies using these mice on aging, adipose tissue, reproduction, metabolism, and cancer. Also, tissue-specific effects on the brain, heart, and bone are reviewed.

Thus, this book is a combination of data obtained in man on the Israeli cohort and the GHR−/−mouse. In each scenario, the action of GH is attenuated resulting in low levels of IGF-I. Similarities and differences between the mouse and human data are pointed out in Chapter 59. The data are both of academic as well as of practical clinical importance.
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