**Prader-Willi Syndrome**

# Endocrine Development

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*Martin O. Savage* *London*

KARGER

# Prader-Willi Syndrome

## Effects of Human Growth Hormone Treatment

*Urs Eiholzer* *Zürich*

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# Foreword

It is a privilege to welcome this outstanding book into the Endocrine Development series. In design, this volume differs from the others in the series in that it is a detailed account of a single disorder, written by a single contributor, Dr. Urs Eiholzer. Dr. Eiholzer and his team in Zürich, where the Prader-Willi syndrome was first described, have devoted the last 10 years to the rigorous clinical and scientific study of this disorder. This book is the result of their painstaking, caring and dedicated approach to this rare, yet extremely important condition.

The volume carefully documents the historical, clinical, behavioural and pathophysiological aspects of the Prader-Willi syndrome. There is a detailed analysis of the endocrine and metabolic abnormalities. Specifically, the growth hormone status of these patients is discussed and the results of the relatively new treatment with recombinant growth hormone are objectively reported with a detailed analysis of potential benefit on growth, body composition and psychomotor development.

This book undoubtedly makes an important contribution to the existing scientific literature concerning the Prader-Willi syndrome. It will be helpful to paediatricians, endocrinologists, educationalists and of course parents concerned with the care of patients with this condition.

London, April 2001 *Martin O. Savage*

# Foreword

The present book by Dr. Eiholzer, published in the renowned Karger *Endocrine Development* Series, is likely to surprise its readership. Besides the outstanding scientific texts, this volume offers comprehensive photographic material to document the development of selected patients over several years. In my view, these photographs illustrate the significant improvement in the children's quality of life better than any text or figure.

In accordance to the treatment plan, our children visited Dr. Eiholzer's private institute twice a year for a half-day consultation. In contrast to the anonymous atmosphere of some of the large clinics, the participants of the study and Dr. Eiholzer with his small team, which remained constant over the years, got to know each other very well during the course of the treatment. The children became accustomed to the examination procedure. To provide Dr. Eiholzer with thorough insight into the daily life of a child with PWS, we shared the development of our children in intimate detail.

Dr. Eiholzer became a member and a focal point of the Swiss PWS community. Children and grown-ups alike became very fond of him. The parents had the invaluable comfort of knowing that highly qualified and understanding support was available when needed. The study also strengthened the bond and mutual support among PWS families and went a long way toward minimizing the feeling of helplessness that sometimes plagues parents.

On behalf of all participants, I thank Dr. Eiholzer for his great commitment in the investigation of PWS. Many other persons with PWS will undoubtedly also benefit from Dr. Eiholzer's findings. I hope that Dr. Eiholzer and his team will continue their work on PWS – since to date, many questions remain open.

*Andreas Bächli,* PhD
Father of Pascal, born 1992 with PWS
President of the Swiss PWS Association

# Preface

In 1991, when I became a member of the then founded Swiss Prader-Willi Syndrome Association, I was deeply impressed by the difficulties these mentally handicapped and obese children were faced with. The mood in the Prader-Willi Association was rather depressed; any outlook or hope for the future were lacking. Treatment was limited to nonspecific measures, mainly reduction of calorie intake, which was only possible by means of strict supervision and permanent locking-up of food. Yet, even close supervision of nutrient intake only contributed to limit obesity, but was not a means to avoid it.

The diagnosis 'Prader-Willi Syndrome' generally shocked parents. When they met adolescents and adults with PWS and learnt that difficulties due to behaviour and disturbed satiation increase with age and persist even through adulthood, they were appalled. Moreover, before the diagnosis of PWS had been established, most parents concerned were suspected by their doctors of not feeding their infants adequately, whereas later, when eating out in a restaurant, people pointed at them with their fingers, asking why they did not stop their child from overeating.

This situation drove us and others to engage in clinical research in PWS and to develop new treatment strategies.

Our focus in designing the studies presented in this book lay on the improvement of the well-being of these children and their families, while we also wanted to gain more knowledge on PWS, in order to be able to offer optimized treatment modalities for the next generation of children and families concerned. It was important to us to keep additional stress for the children and their families as low as possible. We therefore conducted our examinations with a minimum of invasive procedures and patients' time. Furthermore, we wanted to learn as much as possible from the parents – in our view the real experts. The information provided by them was collected and analysed to gain insights into coping with the disease and into favourable ways of bringing up the children concerned.

Over the past years, great advances have been made in treatment options and knowledge about PWS. It was shown that there is a hypothalamic growth hormone deficiency in PWS and that treatment with growth hormone improves body composition, body proportions and physical performance. Increased lean body mass enhances energy expenditure and, provided energy input can be restrained,

children no longer become obese. The disappearance of the obese phenotype of the children that are treated with growth hormone from before puberty on relieves them and their families of stigmatization. The mental retardation and the compulsive behaviour disorder, however, will remain major handicaps and do not seem to be influenced by growth hormone therapy.

This book provides an overview of the clinical research results as to hormones and metabolism of PWS with special emphasis on growth hormone and growth hormone treatment. To illustrate extreme individual changes in the physical appearance and facial expression, this book contains a chapter with a photographic documentation of selected patients.

We will continue our commitment and we firmly hope that most of the information provided in this book will be outdated in a few years' time and be replaced by new insights into Prader-Willi syndrome, to the benefit of all patients with this syndrome.

Zürich, April 2001 *Urs Eiholzer*

# Acknowledgements

We wish to acknowledge the PWS Association of Switzerland and in particular the parents' and children's great commitment and efforts. For providing assistance to obtain the necessary resources, we would like to thank the Foundation Growth Puberty Adolescence.

It is a feeling of great gratitude that I have toward Professor Andrea Prader and Professor Milo Zachmann for their assistance in designing the first study and for introducing a formerly unknown pediatrician to the international scientific community.

The provision of growth hormone and support from Dr. Martin Egli and Pharmacia is also gratefully acknowledged.

An especial debt of gratitude is owed to Dr. Dagmar l'Allemand, pediatric endocrinologist, for the very close and highly productive scientific cooperation.

For her largely independent organisation of the studies and her warm and competent relationship with the patients we are most grateful to Claudia Weinmann.

For the statistical analysis of the results during the early years, we thank Rafael Gisin, lic. rer. pol., and Michael Schlumpf, stud. med., for the follow-up calculations and most of the figures as well as Dr. Luciano Molinari, Zürich, for statistical supervision and his friendly support.

We especially wish to thank Prof. Ken Ellis, Houston, Tex., and Prof. Theo Gasser, Zürich, who, at a decisive and difficult point in time, came to our aid by helping us to understand the changes in body composition and to find the appropriate statistical procedures.

Of course, a special measure of gratitude is due to all the co-authors of the various papers, in particular the heads of the laboratories involved: Dr. Toni Torresani, Zürich; Prof. Walter Riesen, St. Gallen; Dr. Kurt Furrer, Zürich; Prof. Jürg Girard, Basel; PD Dr. Hans Steinert, Zürich; Prof. Jürgen Zapf, Zürich; Prof. Werner Blum, Giessen, Germany. It is remarkable that all the laboratories, including the private ones, performed their laboratory tests free of charge.

We are indebted to Dr. Marius and Dr. Claude Kraenzlin, Basel, for a great number of ideas and suggestions.

We wish to thank Dr. Sara Bachmann, Dr. Yves Nordmann and Dr. Katherina Papageorgiou, Mirella Frey, as well as all co-workers who had all helped us temporarily.

Our grateful thanks are due to Dr. Jürgen Grieser and Dr. Marie-Anne Fritschi, psychologists at our institute, for helping to develop our own comprehensive approach in these patients.

For taking the blood samples, which is particularly difficult in children with Prader-Willi syndrome, we wish to thank Susanne Zimmermann.

We have a special debt to Dr. Eberhard Zangger for the close supervision and quality assurance of the manuscripts, and for his encouragement.

We owe an especial debt of gratitude to Karin Stutz for her assistance in editing all of our papers and this manuscript and Gisela Maranta for the layout.

Special thanks go to Rolf Dinkelmann for the development and implementation of our software systems.

To all our patients we owe the biggest debt of all, because without their input and the suggestions from and discussions with their parents, we would not have been able to develop all the ideas in this book. They would have deserved co-authorship.

Last but not least, I want to express my deep gratitude to my wife, Barbara, and my two sons, Till and Leo, for their understanding and patience during many years and their support in both word and deed.

Zürich, April 2001 *Urs Eiholzer*