Growth Hormone Therapy in Pediatrics – 20 Years of KIGS
Growth Hormone Therapy in Pediatrics

20 Years of KIGS

Editors

Michael B. Ranke  Tübingen
David A. Price  Manchester
Edward O. Reiter  Springfield, Mass.

128 figures and 133 tables, 2007
# Contents

**Contributors** ....................................................................................................................... IX

**Preface** ................................................................................................................................. XV

---

1. **KIGS: Structure and Organization**  
   Patrick Wilton .................................................................................................................. 1

2. **Review**  
   **Assessment of Growth and Puberty**  
   Gary E. Butler ................................................................................................................... 6

3. **KIGS**  
   **Diagnosis of Children with Short Stature: Insights from KIGS**  
   Kenji Fujieda, Toshiaki Tanaka ....................................................................................... 16

4. **KIGS**  
   **Data Analyses within KIGS**  
   Anders Lindberg, Michael B. Ranke .................................................................................. 23

5. **KIGS**  
   **The KIGS Aetiology Classification System**  
   Michael B. Ranke ................................................................................................................ 29

6. **Review**  
   **Growth Hormone Deficiency: Growth Hormone Tests and Growth Hormone Measurements**  
   Susan R. Rose ..................................................................................................................... 38

6. **KIGS**  
   **Growth Hormone Testing in KIGS**  
   Maïthé Tauber .................................................................................................................... 47

7. **Review**  
   **Growth Hormone Deficiency and Modalities of Birth**  
   Angel Ferrández-Longás, Esteban Mayayo, José Ignacio Labarta, Agustin Romo .................. 56

7. **KIGS**  
   **Modalities and Characteristics at Birth: Commentaries Based on KIGS Data**  
   Michael B. Ranke ................................................................................................................ 60

8. **Review**  
   **The Role of Insulin-Like Growth Factors in Growth Hormone Deficiency**  
   Anders Juul .......................................................................................................................... 70

8. **KIGS**  
   **Insulin-Like Growth Factor 1 Levels in Patients within the KIGS Database**  
   Michael B. Ranke ................................................................................................................ 83
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
<th>Title</th>
<th>Authors</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Review</td>
<td>Neuroimaging in Growth Hormone Deficiency</td>
<td>Mohamad Maghnie, Natascia di Iorgi, Andrea Rossi, Roberto Gastaldi, Paolo Tortori-Donati, Renata Lorini</td>
<td>93</td>
</tr>
<tr>
<td>10</td>
<td>Review</td>
<td>Characteristics of Idiopathic Growth Hormone Deficiency at the Start of Growth Hormone Therapy and the Response to Growth Hormone</td>
<td>Herwig Frisch</td>
<td>108</td>
</tr>
<tr>
<td>10</td>
<td>KIGS</td>
<td>Idiopathic Growth Hormone Deficiency in KIGS: Selected Aspects</td>
<td>Michael B. Ranke, Edward O. Reiter, David A. Price</td>
<td>116</td>
</tr>
<tr>
<td>11</td>
<td>Review</td>
<td>Growth Hormone Deficiency: Puberty and Final Height</td>
<td>Edward O. Reiter, Wayne S. Cutfield</td>
<td>136</td>
</tr>
<tr>
<td>11</td>
<td>KIGS</td>
<td>Growth Hormone Treatment to Final Height in Idiopathic Growth Hormone Deficiency: The KIGS Experience</td>
<td>Wayne S. Cutfield, Georgios Karagiannis, Edward O. Reiter</td>
<td>145</td>
</tr>
<tr>
<td>12</td>
<td>Review</td>
<td>The Transition from Childhood to Adulthood: Managing Those with Growth Hormone Deficiency</td>
<td>Helena Gleeson, Peter E. Clayton</td>
<td>163</td>
</tr>
<tr>
<td>12</td>
<td>KIGS</td>
<td>Effect of Prior Pediatric Growth Hormone Replacement on Serum Lipids and Quality of Life in Young Adults with Reconfirmed Severe Growth Hormone Deficiency: The Combined KIGS and KIMS Experiences</td>
<td>Mitchell E. Geffner, Peter Jönsson, John P. Monson, Roger Abs, Václav Hána, Charlotte Höybye, Maria Koltowska-Häggström</td>
<td>176</td>
</tr>
<tr>
<td>13</td>
<td>KIGS</td>
<td>Who Stops Growth Hormone in KIGS – and Why?</td>
<td>Michael B. Ranke</td>
<td>183</td>
</tr>
<tr>
<td>14</td>
<td>Review</td>
<td>Congenital Growth Hormone Deficiency</td>
<td>Primus E. Mullis</td>
<td>189</td>
</tr>
<tr>
<td>14</td>
<td>KIGS</td>
<td>Growth Hormone Deficiency of Known Origin within KIGS (Code No. 2.1.1–2.1.6)</td>
<td>Michael B. Ranke, Hanna Karlsson</td>
<td>202</td>
</tr>
<tr>
<td>15</td>
<td>Review/KIGS</td>
<td>Growth Hormone Treatment of Children with Previous Craniopharyngioma: The KIGS Experience</td>
<td>David A. Price</td>
<td>207</td>
</tr>
<tr>
<td>16</td>
<td>Review/KIGS</td>
<td>Growth Hormone Treatment in Rare Disorders: The KIGS Experience</td>
<td>Feyza Darendeliler</td>
<td>213</td>
</tr>
<tr>
<td>17</td>
<td>Review</td>
<td>Childhood Brain Tumours and Growth Hormone Treatment</td>
<td>Andreas Jostel, Stephen M. Shalet</td>
<td>240</td>
</tr>
<tr>
<td>17</td>
<td>KIGS</td>
<td>KIGS Patients with Acquired Growth Hormone Deficiency (Code No. 2.2 ff.)</td>
<td>Michael B. Ranke</td>
<td>250</td>
</tr>
<tr>
<td>18</td>
<td>KIGS</td>
<td>Growth Hormone Treatment of Children with Previous Leukaemia and Lymphoma: The KIGS Experience</td>
<td>David A. Price, Hanna Karlsson</td>
<td>261</td>
</tr>
<tr>
<td>Page</td>
<td>Type</td>
<td>Title</td>
<td>Authors</td>
<td>Page</td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
<td>--------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>19</td>
<td>Review</td>
<td>Growth Hormone, Langerhans Cell Histiocytosis and Neurofibromatosis</td>
<td>Michel Polak</td>
<td>269</td>
</tr>
<tr>
<td>19</td>
<td>KIGS</td>
<td>Growth Hormone Treatment in Neurofibrosis Type 1 Involving Central Nervous System Tumours and Pituitary Langerhans Cell Histiocytosis within KIGS</td>
<td>Michael B. Ranke, Wayne S. Cutfield</td>
<td>277</td>
</tr>
<tr>
<td>20</td>
<td>Review</td>
<td>Growth and GH Treatment in Patients with Juvenile Idiopathic Arthritis</td>
<td>Paul Czernichow</td>
<td>286</td>
</tr>
<tr>
<td>20</td>
<td>KIGS</td>
<td>The KIGS Experience with Growth Hormone Treatment of Juvenile Rheumatoid Arthritis</td>
<td>Edward O. Reiter</td>
<td>292</td>
</tr>
<tr>
<td>21</td>
<td>Review</td>
<td>Cystic Fibrosis – Growth Hormone Treatment</td>
<td>Dirk Schnabel</td>
<td>296</td>
</tr>
<tr>
<td>21</td>
<td>KIGS</td>
<td>The KIGS Experience with Growth Hormone Treatment of Cystic Fibrosis</td>
<td>Edward O. Reiter</td>
<td>304</td>
</tr>
<tr>
<td>22</td>
<td>Review</td>
<td>Idiopathic Short Stature: Definition, Spontaneous Growth and Response to Treatment</td>
<td>Jan M. Wit</td>
<td>309</td>
</tr>
<tr>
<td>23</td>
<td>Review</td>
<td>Turner Syndrome – Growth Hormone Treatment</td>
<td>Ron G. Rosenfeld</td>
<td>326</td>
</tr>
<tr>
<td>23</td>
<td>KIGS</td>
<td>Turner Syndrome within KIGS Including an Analysis of 1146 Patients Grown to Near Adult Height</td>
<td>Michael B. Ranke, Anders Lindberg</td>
<td>332</td>
</tr>
<tr>
<td>24</td>
<td>Review</td>
<td>Noonan Syndrome</td>
<td>Christopher J.H. Kelnar</td>
<td>340</td>
</tr>
<tr>
<td>24</td>
<td>KIGS</td>
<td>Short Stature in Noonan Syndrome: Results of Growth Hormone Treatment in KIGS</td>
<td>Barto J. Otten, Kees Noordam</td>
<td>347</td>
</tr>
<tr>
<td>25</td>
<td>Review/KIGS</td>
<td>Growth Hormone Treatment in Skeletal Dysplasias: The KIGS Experience</td>
<td>Thomas Hertel</td>
<td>356</td>
</tr>
<tr>
<td>26</td>
<td>Review</td>
<td>Prader-Willi Syndrome and Growth Hormone Treatment</td>
<td>Ann Christin Lindgren</td>
<td>369</td>
</tr>
<tr>
<td>26</td>
<td>KIGS</td>
<td>Effects of Growth Hormone Treatment in Children Presenting with Prader-Willi Syndrome: The KIGS Experience</td>
<td>Maithé Tauber</td>
<td>377</td>
</tr>
<tr>
<td>Page</td>
<td>Type</td>
<td>Title</td>
<td>Authors</td>
<td>Pages</td>
</tr>
<tr>
<td>------</td>
<td>------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>27</td>
<td>Review</td>
<td>Growth and Growth Hormone Treatment in Children Born Small for Gestational Age and with Silver-Russell Syndrome</td>
<td>Wayne S. Cutfield, Edward O. Reiter on behalf of the KIGS International Board</td>
<td>389</td>
</tr>
<tr>
<td>27</td>
<td>KIGS</td>
<td>KIGS 20 Years: Children Born Small for Gestational Age</td>
<td>David B. Dunger</td>
<td>400</td>
</tr>
<tr>
<td>29</td>
<td>Review/KIGS</td>
<td>Predicting Growth in Response to Growth Hormone Treatment – The KIGS Approach</td>
<td>Michael B. Ranke, Anders Lindberg</td>
<td>422</td>
</tr>
<tr>
<td>30</td>
<td>Review/KIGS</td>
<td>Adverse Events Reported in KIGS</td>
<td>Patrick Wilton</td>
<td>432</td>
</tr>
<tr>
<td>31</td>
<td>Review</td>
<td>Progress and Challenges in Understanding the Psychology of Growth Delay</td>
<td>Brian Stabler, Louis E. Underwood</td>
<td>442</td>
</tr>
<tr>
<td>32</td>
<td>Review</td>
<td>Growth Hormone and Brain Function</td>
<td>Fred Nyberg</td>
<td>450</td>
</tr>
<tr>
<td>33</td>
<td>Review</td>
<td>Review of Methods for Body Composition Assessment in Children</td>
<td>Jonathan C.K. Wells</td>
<td>461</td>
</tr>
<tr>
<td>34</td>
<td>Review</td>
<td>Metabolic Effects of Growth Hormone</td>
<td>Ulla Feldt-Rasmussen</td>
<td>477</td>
</tr>
<tr>
<td>35</td>
<td>Review</td>
<td>The Growth Plate</td>
<td>Ola Nilsson</td>
<td>485</td>
</tr>
<tr>
<td>36</td>
<td>Review</td>
<td>Pharmacogenetics of Growth Hormone Therapy</td>
<td>Linda B. Johnston, Adrian J.L. Clark</td>
<td>500</td>
</tr>
</tbody>
</table>

Author Index .......................................................... 509
Subject Index ........................................................ 511
Contributors

**Dr. Roger Abs**
Department of Endocrinology
University Hospital Antwerp
Wilrijkstraat 10
BE–2650 Edegem (Belgium)
Tel. +32 3 821 3885
Fax +32 3 821 4185
E-Mail roger.abs@uza.be

**Prof. Kerstin Albertsson-Wikland**
Paediatric Growth Research Centre
Department of Paediatrics
Queen Silvia Children's Hospital
Sahlgrenska Academy of Gothenburg University
SE–416 85 Gothenburg (Sweden)
Tel. +46 31 343 5165
Fax +46 31 848 952
E-Mail kerstin.albertsson-wikland@pediat.gu.se

**Prof. Gary E. Butler**
Department of Paediatrics and Growth Institute of Health Sciences
University of Reading
London Road
Reading RG1 5AQ (United Kingdom)
Tel. +44 118 378 6863
Fax +44 118 378 6862
E-Mail g.e.butler@reading.ac.uk

**Prof. Adrian J.L. Clark**
Department of Endocrinology
William Harvey Research Unit
Charterhouse Square
Barts and the London Queen Mary School of Medicine
London EC1M 6BQ (United Kingdom)
Tel. +44 207 601 7078
Fax +44 207 601 8505
E-Mail a.j.clark@qmul.ac.uk

**Prof. Peter E. Clayton**
Department of Child Health and Paediatric Endocrinology
University of Manchester
Oxford Road
Manchester M13 9PT
(United Kingdom)
Tel. +44 161 922 2585
Fax +44 161 922 2583
E-Mail peter.clayton@manchester.ac.uk

**Prof. Wayne S. Cutfield**
Liggins Institute
University of Auckland
2-6 Park Avenue
Grafton, Auckland (New Zealand)
Tel. +64 9 373 7599 (ext. 84476)
Fax +64 9 373 7497
E-Mail w.cutfield@auckland.ac.nz

**Prof. Paul Czernichow**
Department of Endocrinology and Growth Diseases
Hôpital Necker
149 rue de Sévres
FR–75015 Paris (France)
Tel. +33 1 44 49 48 01
Fax +33 1 44 49 48 00
E-Mail paul.czernichow@nck.aphp.fr

**Prof. Feyza Darendeliler**
Department of Pediatrics
Istanbul Faculty of Medicine
Istanbul University
TR–34390 Capa – Istanbul (Turkey)
Tel. +90 212 635 11 89
Fax +90 212 533 13 83
E-Mail feyzad@istanbul.edu.tr

**Prof. David B. Dunger**
Department of Paediatrics
Addenbrooke’s Hospital
University of Cambridge
Hills Road, Level 8, Box 116
Cambridge CB2 2QZ
(United Kingdom)
Tel. +44 1223 726 944
Fax +44 1223 336 996
E-Mail dbd25@cam.ac.uk
Prof. Ulla Feldt-Rasmussen
Department of Medical Endocrinology PE-2132 Rigshospitalet Copenhagen University Hospital Blegdamsvej 9 DK–2100 Copenhagen (Denmark) Tel. +45 35 45 23 37 Fax +45 35 45 22 40 E-Mail ufeldt@rh.dk

Dr. Roberto Gastaldi
Department of Pediatrics IRCCS Giannina Gaslini University of Genova Largo Gerolamo Gaslini 5 IT–16147 Genova (Italy) Tel. +39 010 563 6691 Fax +39 010 377 6778 E-Mail gastaldiro@hotmail.com

Dr. Václav Hána
3rd Department of Internal Medicine Faculty of Medicine 1 Charles University U nemocnice 1 CZ–128 08 Prague 2 (Czech Republic) Tel. +420 22496 2919 Fax +420 22491 9780 E-Mail vhana@lf1.cuni.cz

Dr. Thomas Hertel
Department of Paediatrics Odense University Hospital Sdr. Boulevard 29 DK–5000 Odense C (Denmark) Tel. +45 65 41 45 60 Fax +45 65 911 862 E-Mail thomas.hertel@ouh.fyns-amt.dk

Prof. Angel Ferrández-Longás
Hospital Infantil Universitario Miguel Servet Av. Isabel la Católica 3 ES–50009 Zaragoza (Spain) Tel. +34 976 765 649 Fax +34 976 765 633 E-Mail aferrandezl@salud.aragon.es

Dr. Mitchell E. Geffner
The Saban Research Institute Children’s Hospital Los Angeles 4650 Sunset Blvd. Los Angeles, CA 90027 (USA) Tel. +1 323 669 7032 Fax +1 323 953 1349 E-Mail mgeffner@chla.usc.edu

Dr. Charlotte Höybye
Department of Endocrinology, Metabolism and Diabetes Karolinska University Hospital SE–171 76 Stockholm (Sweden) Tel. +46 8 517 75379 Fax +46 8 517 73096 E-Mail charlotte.hoybye@karolinska.se

Prof. Herwig Frisch
St. Anna Children’s Hospital Kinderspitalgasse 6 AT–1090 Vienna (Austria) Tel. +43 1 401 700 Fax +43 1 401 70 710 E-Mail herwig.frisch@meduniwien.ac.at

Dr. Charlene Gleeson
Department of Endocrinology Christie Hospital NHS Trust Wilmslow Road Withington Manchester M20 4BX (United Kingdom) Tel. +44 161 860 0696 Fax +44 161 446 3772 E-Mail helena.gleeson@btinternet.com

Prof. Kenji Fujieda
Department of Pediatrics Asahikawa Medical College 2-1-1 Midorigaoka, Higashi Asahikawa 078-8510, Hokkaidou (Japan) Tel. +81 166 682 481 Fax +81 166 682 489 E-Mail ken-fuji@asahikawa-med.ac.jp

Dr. Dieter Haffner
University Hospital of Pediatric and Adolescent Medicine Rembrandtstrasse 17–18 DE–18075 Rostock (Germany) Tel. +49 381 494 7001 Fax +49 381 494 7002 E-Mail dieter.haffner@med.uni-rostock.de

Prof. Natascia di Iorgi
Department of Pediatrics IRCCS Giannina Gaslini University of Genova Largo Gerolamo Gaslini 5 IT–16147 Genova (Italy) Tel. +39 010 563 6002 Fax +39 010 377 6778 E-Mail natasciadiiorgi@ospedale-gaslini.ge.it
Mr. Peter Jönsson
Pfizer Endocrine Care
KIGS/KIMS/ACROSTUDY
Medical Outcomes
Vetenskapsvägen 10
SE–191 90 Sollentuna (Sweden)
Tel. +46 8 550 529 34
Fax +46 8 550 526 80
E-Mail peter.j.jonsson@pfizer.com

Mr. Georgios Karagiannis
Pfizer Endocrine Care
KIGS/KIMS/ACROSTUDY
Medical Outcomes
Vetenskapsvägen 10
SE–191 90 Sollentuna (Sweden)
Tel. +46 8 550 529 38
Fax +46 8 550 526 80
E-Mail georgios.karagiannis@pfizer.com

Prof. José Ignacio Labarta
Hospital Infantil Universitario Miguel Servet
Av. Isabel la Católica 3
ES–50009 Zaragoza (Spain)
Tel. +34 976 765 500 (ext. 3475)
Fax +34 976 566 234
E-Mail jilabarta@solunet.es

Dr. Linda B. Johnston
Department of Endocrinology
William Harvey Research Unit
John Vane Science Centre
Charterhouse Square
Barts and the London Queen Mary School of Medicine
London EC1M 6BQ (United Kingdom)
Tel. +44 20 7882 6242
Fax +44 20 7882 6197
E-Mail l.b.johnston@qmul.ac.uk

Dr. Anders Jostel
Department of Endocrinology
Christie Hospital
Wilmslow Road
Manchester M20 4BX
(United Kingdom)
Tel. +44 161 446 3668
Fax +44 161 446 3772
E-Mail andreas.jostel@man.ac.uk

Ms. Hanna Karlsson
Pfizer Endocrine Care
KIGS/KIMS/ACROSTUDY
Medical Outcomes
Vetenskapsvägen 10
SE–191 90 Sollentuna (Sweden)
Tel. +46 8 550 529 39
Fax +46 8 550 526 80
E-Mail hanna.karlsson@pfizer.com

Dr. Ann Christin Lindgren
Pediatric Endocrinology Unit
Department of Woman and Child Health
Astrid Lindgren Children’s Hospital
Karolinska Hospital
SE–171 76 Stockholm (Sweden)
Tel. +46 733 380 816
Fax +46 8 517 777 39
E-Mail ann.christin.lindgren@ki.se

Dr. Anders Juul
University Department of Growth and Reproduction
Rigshospitalet, Section 5064
Blegdamsvej 9
DK–2100 Copenhagen (Denmark)
Tel. +45 35 45 5085
Fax +45 35 45 6054
E-Mail ajuul@rh.dk

Dr. Maria Koltowska-Häggström
Pfizer Endocrine Care
KIGS/KIMS/ACROSTUDY
Medical Outcomes
Vetenskapsvägen 10
SE–191 90 Sollentuna (Sweden)
Tel. +46 8 550 529 16
Fax +46 8 550 526 80
E-Mail maria.koltowska-haggstrom@pfizer.com

Dr. Renata Lorini
Department of Pediatrics
IRCCS Giannina Gaslini
University of Genova
Largo Gerolamo Gaslini 5
IT–16147 Genova (Italy)
Tel. +39 010 563 6654
Fax +39 010 377 3210
E-Mail renatalorini@ospedale-gaslini.ge.it

Prof. Christopher J.H. Kelnar
Department of Paediatric Endocrinology
Section of Child Life and Health
University of Edinburgh
20 Sylvan Place
Edinburgh EH9 1UW (United Kingdom)
Tel. +44 131 536 0611
Fax +44 131 536 0821
E-Mail chris@kelnar.com

Mr. Georgios Karagiannis
Pfizer Endocrine Care
KIGS/KIMS/ACROSTUDY
Medical Outcomes
Vetenskapsvägen 10
SE–191 90 Sollentuna (Sweden)
Tel. +46 8 550 529 38
Fax +46 8 550 526 80
E-Mail georgios.karagiannis@pfizer.com

Mr. José Ignacio Labarta
Hospital Infantil Universitario Miguel Servet
Av. Isabel la Católica 3
ES–50009 Zaragoza (Spain)
Tel. +34 976 765 500 (ext. 3475)
Fax +34 976 566 234
E-Mail jilabarta@solunet.es

Dr. Anders Jostel
Department of Endocrinology
Christie Hospital
Wilmslow Road
Manchester M20 4BX
(United Kingdom)
Tel. +44 161 446 3668
Fax +44 161 446 3772
E-Mail andreas.jostel@man.ac.uk

Dr. Maria Koltowska-Häggström
Pfizer Endocrine Care
KIGS/KIMS/ACROSTUDY
Medical Outcomes
Vetenskapsvägen 10
SE–191 90 Sollentuna (Sweden)
Tel. +46 8 550 529 16
Fax +46 8 550 526 80
E-Mail maria.koltowska-haggstrom@pfizer.com

Dr. Renata Lorini
Department of Pediatrics
IRCCS Giannina Gaslini
University of Genova
Largo Gerolamo Gaslini 5
IT–16147 Genova (Italy)
Tel. +39 010 563 6654
Fax +39 010 377 3210
E-Mail renatalorini@ospedale-gaslini.ge.it

Mr. Anders Lindberg
Pfizer Endocrine Care
KIGS/KIMS/ACROSTUDY
Medical Outcomes
Vetenskapsvägen 10
SE–191 90 Sollentuna (Sweden)
Tel. +46 8 550 529 37
Fax +46 8 550 526 80
E-Mail anders.lindberg@pfizer.com
Since its inception in 1987, KIGS (Pfizer International Growth Database) has established itself as a major pharmacoepidemiological survey investigating growth hormone (GH) treatment in children with short stature. Today, more than 62,000 patients from more than 50 countries are enrolled in KIGS, and a considerable number of them have been followed to final height. Over the years, KIGS has become a major source of documentation of growth disorders and their treatment with recombinant GH.

During the past 20 years, the worldwide social, economical and medical structures have changed considerably. The idea of evidence-based medicine, which was part of the founding idea of KIGS, has become a globally accepted principle. The increasingly available information as a result of the new and ubiquitously available media has created a higher level of information and openness in the world of medicine and the public domain. With regard to GH, our understanding of its role in child development beyond growth and our concepts of treatment have expanded. Several new indications for GH treatment, such as chronic renal insufficiency, Prader-Willi syndrome and small for gestational age, were added to its traditional role of replacement in various forms of GH deficiency. The effects of GH on body composition, metabolism and child development have been recognised as additional important elements of GH treatment. The concept of responsiveness has emerged, and today, as a consequence of the development of new treatment algorithms, GH therapy can be individualised and optimised. The KIGS system has, by various means, accompanied, promoted and documented all of these developments over the past 20 years.

The present volume attempts to expand on the accounts given in the books published after 5 and 10 years. We are grateful for the contributions of many experts who have summarised the global experience in a multiplicity of areas of growth and GH treatment. Part of the extensive information accumulated in the KIGS database was analysed and gives an additional reflection of the various aspects from within KIGS. We hope that all of this information will stimulate the participants within KIGS to further support this unique and evolving quest to improve the long-term efficacy and safety of GH treatment in children and adolescents.

The editors are grateful for the continuing support and encouragement by Pfizer and the KIGS team, in particular Margaretha Lindell, Anders Lindberg, Georgios Karagiannis and Hanna Karlsson who have made the realisation of this book possible. We would also like to express our gratitude for the encouragement and endorsement the KIGS project received from Annika Wallström, Rolf Gunnarsson, Olivier Guilbaud and Patrick Wilton. We greatly appre-
ciate the scientific support of the members of the Strategic Advisory Board: Kerstin Albertsson-Wikland, Magda Vanderschueren-Lodeweyckx, Pierre Chatelain, Marc Maes, Wayne Cutfield, Chris Cowell, Feyza Darendeliler, Angel Ferrandez-Longas, Maithé Tauber, David Dunger and Mitchell Geffner. In particular, we would like to acknowledge the efforts taken by all participating physicians in contributing data for the analyses within KIGS. We are also grateful to Karger for their committed editorial support.

Michael B. Ranke, Tübingen, Germany
David A. Price, Manchester, UK
Edward O. Reiter, Springfield, Mass., USA