Androgens in Gynecological Practice
Androgens in Gynecological Practice

Edited by

Leo Plouffe Jr. MD CM FACOG FRCS(C)
Vice President, Global Pharmacovigilance, and Head, Risk Management, Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA

Botros R. M. B. Rizk MD MA FRCOG FRCS HCLD FACOG FACS
Professor of Obstetrics and Gynecology, and Director of the Division of Reproductive Endocrinology and Infertility, University of South Alabama, Mobile, AL, USA
## Contents

**About the editors** vii  
**Dedication** viii  
**List of contributors** ix  
**Preface** xi

### Section 1 – Managing the basics

1. **Hirsutism: managing the basics**  
   Héctor F. Escobar-Morreale

2. **Alopecia: managing the basics**  
   Thamer Mubki and Jerry Shapiro

3. **Polycystic ovary syndrome: managing the basics**  
   Keith A. Hansen

4. **Sexual dysfunction, including hypoactive sexual desire disorder: diagnosis and treatment recommendations**  
   Ricki Pollycove and James A. Simon

### Section 2 – The scientific essentials

5. **The androgen receptor: basic structure and function**  
   Leo Plouffe Jr.

6. **Androgens in postmenopausal women: their practically exclusive intracrine formation and inactivation in peripheral tissues**  
   Fernand Labrie

7. **Diagnostic criteria of polycystic ovary syndrome**  
   Heather R. Burks and Robert A. Wild

8. **Androgen effects on the skin**  
   Grace E. Kim and Alexa B. Kimball

9. **Polycystic ovary syndrome and cardiovascular risk**  
   Heather R. Burks and Robert A. Wild

10. **Effects of androgens on female genital tract**  
    Abdumaged M. Traish and André T. Guay

### Section 3 – Learning from the extremes

11. **Congenital adrenal hyperplasia in females**  
    Candice P. Holliday and Botros R. M. B. Rizk

12. **Cushing's syndrome in females**  
    Andrew S. Fischer, Christopher B. Rizk, and Sylvia Hsu

13. **Androgen-producing ovarian tumors**  
    Patricia Carney

14. **Cognitive and behavioral impact of androgen disorders in females: learning from complete androgen insensitivity syndrome and congenital adrenal hyperplasia**  
    Amy B. Wisniewski

15. **Testosterone replacement in the aging male: lessons learned from the Women's Health Initiative**  
    David Muram and Craig F. Donatucci

### Section 4 – The tool kit

16. **History and physical examination of polycystic ovary syndrome: detecting too much or too little**  
    John J. Kohorst, Andrew S. Fischer, and Christopher B. Rizk

17. **Androgen assays: of mice and men**  
    Keith A. Hansen
Contents

18. Magnetic resonance imaging of the adrenal gland 191
   Sajal S. Pokharel and Ihab R. Kamel

19. Androgens and DHEA in postmenopausal medicine 200
   Lila E. Nachtigall and Jeffrey A. Goldstein

20. Lifestyle, diet, and exercise in polycystic ovary syndrome 208
   Elizabeth Burt and Rina Agrawal

21. Polycystic ovary syndrome ovulation induction 216
   Carolyn J. Alexander

22. Ovulation induction in women with polycystic ovary syndrome 226
   Shawky Z. A. Badawy and Botros R. M. B. Rizk

Index 233

The color plate section can be found between pages 116 and 117.
About the editors

Leo Plouffe, MD CM is currently Vice President, Head of Risk Management, Global Pharmacovigilance at Bayer Health Care Pharmaceuticals following his tenure as Head of Women's Health Care US Medical Affairs, also at Bayer. Dr Plouffe started his career as a research scientist over 25 years ago at the Medical College of Georgia, department of Obstetrics and Gynecology, Reproductive Endocrinology and Genetics Section. He achieved the rank of tenured professor before joining Eli Lilly Pharmaceuticals, where he held positions of increasing responsibility in medical affairs and clinical development.

His research interests encompass pediatric and adolescent gynecology, menopausal medicine, contraception, and patient safety. He has authored over 100 scientific papers, book chapters, and abstracts. He is past vice-president of the North American Society for Pediatric and Adolescent Gynecology, and has served on a number of committees and special interest groups at ASRM, ACOG, and SGI. He is a reviewer for several journals in women's health.

Botros R. M. B. Rizk, MD is Professor and Chief of the Division of Reproductive Endocrinology and Infertility of the Department of Obstetrics and Gynecology at the University of South Alabama, Mobile, AL, USA. He is also Program Director and Medical and Scientific Director of the USA IVF and ART Program, and Laboratory Director and Clinical Consultant at the Reproductive Endocrinology Laboratory of the University of South Alabama.

Professor Rizk has worked as a research scientist and clinician in reproductive medicine for more than 25 years. His main research interests include the modern management, prediction, and the genetics of ovarian hyperstimulation syndrome (OHSS), as well as the role of vascular endothelial growth factor and interleukins in the pathogenesis of severe OHSS. He has authored more than 300 peer-reviewed published papers, book chapters, and abstracts. Professor Rizk has edited and authored 18 medical textbooks on OHSS, infertility and assisted reproduction, endometriosis, ultrasonography in reproductive medicine, ovarian stimulation, and the future of ART.

He is past chair of the ASRM international membership committee, member of the scientific advisory board of the Mediterranean Society for Reproductive Medicine, President Elect of the Middle East Fertility Society, on the editorial board of the Middle East Fertility Society Journal, and reviewer for several national and international journals, as well as for the European Society of Human Reproduction and Embryology Task Force on perinatal outcome and congenital malformations of intracytoplasmic sperm injection.
Dedication

To my mentors on this subject, Drs Morrie M. Gelfand, Robert B. Greenblatt, Robert AH Kinch and Paul G. McDonough.

From Drs Gelfand and Greenblatt, I received the passion and enthusiasm to study this topic. From Drs Kinch and McDonough, I received the skillset and discipline to apply evidence-based medicine in the care of these patients.

On a personal level, to my wife Eve, who has supported me through this project as she has through every step of our life journey.

*Leo Plouffe Jr.*

To the RIZK family for their tremendous contribution to Egypt; my great grandfather Rizk Ghobrial Rizk appointed the Governor of East Delta by Mohamed Ali in 1814, my grandfather Botros Rizk after whom I was named, my father Mitry Botros Rizk, and all the uncles and cousins.

*Botros R. M. B. Rizk*

Chapter 10 is dedicated to the memory of my dear friend and colleague Andre T. Guay, MD and for his immense contributions to the advancement of clinical endocrinology, especially sexual function in men and women.

*Abdulmaged M. Traish*
Contributors

Rina Agrawal MD PhD
Centre for Reproductive Medicine, London, UK

Carolyn J. Alexander MD
Department of Obstetrics & Gynecology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Shawky Z. A. Badawy MD
Department of Obstetrics & Gynecology, SUNY Upstate Medical University, Syracuse, NY, USA

Heather R. Burks MD
Department of Obstetrics & Gynecology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

Elizabeth Burt MBBS
University College London, London, UK

Patricia Carney MD
Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA

Craig F. Donatucci MD
Division of Urology, Duke University Medical Center, Durham, NC, USA

Héctor F. Escobar-Morreale MD PhD
Department of Endocrinology & Nutrition; Hospital Universitario Ramón y Cajal, Universidad de Alcalá, IRYCIS, CIBERDEM, Madrid, Spain

Andrew S. Fischer
Baylor College of Medicine, Houston, TX, USA

Jeffrey A. Goldstein DO
Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA

André T. Guay MD
Center for Sexual Function, Lahey Clinic Northshore, Peabody, MA, USA

Keith A. Hansen MD
Department of Obstetrics & Gynecology, University of South Dakota Sanford School of Medicine, Sioux Falls, SD, USA

Candice P. Holliday JD
Department of Obstetrics & Gynecology, University of South Alabama, Mobile, AL, USA

Sylvia Hsu MD
Department of Dermatology, Baylor College of Medicine, Houston, TX, USA

Ihab R. Kamel MD PhD
Department of Radiology & Radiological Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Grace E. Kim BS
Harvard Medical School, Boston, MA, USA

Alexa B. Kimball MD MPH
Department of Dermatology, Massachusetts General Hospital, Boston, MA, USA

John J. Kohorst BA
Mayo Medical School, Rochester, MN, USA

Fernand Labrie MD PhD
Molecular Endocrinology & Oncology Research Center, Laval University Hospital, Québec City, Québec, Canada

Thamer Mubki MD
Department of Dermatology, Al Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia
<table>
<thead>
<tr>
<th>List of contributors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>David Muram MD</strong></td>
</tr>
<tr>
<td>Eli Lilly &amp; Company, Lilly Corporate Center, Indianapolis, IN, USA</td>
</tr>
<tr>
<td><strong>Eli Lilly &amp; Company, Lilly Corporate Center, Indianapolis, IN, USA</strong></td>
</tr>
<tr>
<td><strong>Lila E. Nachtigall MD</strong></td>
</tr>
<tr>
<td>Department of Obstetrics &amp; Gynecology, NYU School of Medicine, New York, NY, USA</td>
</tr>
<tr>
<td><strong>Leo Plouffe Jr. MD CM</strong></td>
</tr>
<tr>
<td>Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA</td>
</tr>
<tr>
<td><strong>Sajal S. Pokharel MD PhD</strong></td>
</tr>
<tr>
<td>Department of Radiology, University of Colorado School of Medicine, Aurora, CO, USA</td>
</tr>
<tr>
<td><strong>Ricki Pollycove MD</strong></td>
</tr>
<tr>
<td>Department of Obstetrics, Gynecology and Reproductive Sciences, CPMC, and VCF Department of Psychiatry, University of California San Francisco, San Francisco, CA, USA</td>
</tr>
<tr>
<td><strong>Botros R. M. B. Rizk MD MA</strong></td>
</tr>
<tr>
<td>Department of Obstetrics &amp; Gynecology, University of South Alabama, Mobile, AL, USA</td>
</tr>
<tr>
<td><strong>Christopher B. Rizk BA</strong></td>
</tr>
<tr>
<td>Baylor Medical College, Houston, TX</td>
</tr>
<tr>
<td><strong>Jerry Shapiro MD</strong></td>
</tr>
<tr>
<td>Department of Dermatology, New York University Langone Medical Center, New York City, NY, USA</td>
</tr>
<tr>
<td><strong>James A. Simon MD</strong></td>
</tr>
<tr>
<td>Department of Obstetrics &amp; Gynecology, George Washington University School of Medicine, Washington, DC, USA</td>
</tr>
<tr>
<td><strong>Abdulmaged M. Traish PhD</strong></td>
</tr>
<tr>
<td>Institute of Sexual Medicine, Boston University School of Medicine, Boston, MA, USA</td>
</tr>
<tr>
<td><strong>Robert A. Wild MD PhD MPH</strong></td>
</tr>
<tr>
<td>Department of Obstetrics &amp; Gynecology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA</td>
</tr>
<tr>
<td><strong>Amy B. Wisniewski PhD</strong></td>
</tr>
<tr>
<td>Department of Urology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA</td>
</tr>
</tbody>
</table>
A wide range of disease states that affect women are associated with dysfunctional androgen production, either deficiency or excess states. This encompasses common disorders, such as polycystic ovary syndrome (PCOS) or acne and hirsutism, as well as rare conditions, such as congenital adrenal hyperplasia. Thousands of original scientific publications and hundreds of scholarly books have covered these conditions over the years. Why does the medical community need one more book on the subject?

In reviewing the available reference sources, we were struck that the underlying theme was focusing on the specific medical conditions affecting women, and working back to the underlying androgen dysregulation associated with the condition. This is an extremely valuable approach and has served the practitioner very well over the years. However, it is often helpful to consider a new perspective to stimulate new insights into a medical problem. How could we bring about an element of novelty?

What if we first focused on androgens and considered how they impact normal physiology, from the receptor all the way to the entire body? What if we focused on a variety of androgens, at the biochemical level and their respective physiological impact? What if we considered androgen effects not just in women but also in men? What about seeing how much we can learn from the endocrinology of androgens in rare androgen-linked conditions that we can apply to our understanding in the care of all women? What can medical practitioners with a wide range of specialty and clinical backgrounds learn from one another in a scientific forum? We thought such an approach may help reframe many of the issues of androgens in women’s health.

This book represents an amazing collaboration of scientists that bought in to our novel approach, and agreed to participate in this experiment. We reached out to many specialists in the field. All of the contributing authors valued the opportunity and provided their unique and crisp insights in a way that we hope will open up new ideas, and hopefully drive further scientific progress.

At the same time, we wanted to make sure this book would be of practical value for every clinician. The clinical chapters provide a clear framework to work-up and manage patients. They are complemented by many chapters on the intricacies of making an accurate diagnosis, also essential for the clinician. And last but not least, the remaining chapters provide highly relevant insights into the scientific underpinnings of these complex conditions.

We hope you will find this book valuable and consult it frequently. Above all, we hope it will help you take even better care of your patients, and for some of you, trigger new research ideas.

Good reading.
Leo Plouffe Jr
Botros R. M. B. Rizk