
**THE POLYCYSTIC
OVARY SYNDROME:**

**CURRENT CONCEPTS
ON PATHOGENESIS AND
CLINICAL CARE**

ENDOCRINE UPDATES

Shlomo Melmed, M.D., Series Editor

- J.S. Adams and B.P. Lukert (eds.): Osteoporosis: Genetics, Prevention and Treatment. 1998. ISBN 0-7923-8366-4.
- B.-Å. Bengtsson (ed.): Growth Hormone. 1999. ISBN 0-7923-8478-4
- C. Wang (ed.): Male Reproductive Function. 1999. ISBN 0-7923-8520-9
- B. Rapoport and S.M. McLachlan (eds.): Graves' Disease: Pathogenesis and Treatment. 2000. ISBN 0-7923-7790-7.
- W.W. de Herder (ed.): Functional and Morphological Imaging of the Endocrine System. 2000. ISBN 0-7923-7923-9
- H.G. Burger (ed.): Sex Hormone Replacement Therapy. 2001. ISBN 0-7923-7965-9
- A. Giustina (ed.): Growth Hormone and the Heart. 2001. ISBN 0-7923-7212-3
- W.L. Lowe, Jr. (ed.): Genetics of Diabetes Mellitus. 2001. ISBN 0-7923-7252-2
- J.F. Habener and M.A. Hussain (eds.): Molecular Basis of Pancreas Development and Function. 2001. ISBN 0-7923-7271-9
- N. Horseman (ed.): Prolactin. 2001. ISBN 0-7923-7290-5
- M. Castro (ed.): Transgenic Models in Endocrinology. 2001. ISBN 0-7923-7344-8
- R. Bahn (ed.): Thyroid Eye Disease. 2001. ISBN 0-7923-7380-4
- M.D. Bronstein (ed.): Pituitary Tumors in Pregnancy ISBN 0-7923-7442-8
- K. Sandberg and S.E. Mulroney (eds.): RNA Binding Proteins: New Concepts in Gene Regulation. 2001. ISBN 0-7923-7612-9
- V. Goffin and P.A. Kelly (eds.): Hormone Signaling. 2002. ISBN 0-7923-7660-9
- M.C. Sheppard and P.M. Stewart (eds.): Pituitary Disease. 2002. ISBN 1-4020-7122-1
- N. Chattopadhyay and E.M. Brown (eds.): Calcium-Sensing Receptor. 2002. ISBN 1-4020-7314-3
- H. Vaudry and A. Arimura (eds.): Pituitary Adenylate Cyclase-Activating Polypeptide. 2002. ISBN 1-4020-7306-2
- R.C. Gaillard (ed.): The ACTH AXIS: Pathogenesis, Diagnosis and Treatment. 2003. ISBN 1-4020-7563-4
- P. Beck-Peccoz (ed.): Syndromes of Hormone Resistance on the Hypothalamic-Pituitary-Thyroid Axis. 2004. ISBN 1-4020-7807-2
- E. Ghigo (ed.): Ghrelin. 2004. ISBN 1-4020-7770-X
- C.B. Srikant (ed.): Somatostatin. 2004. ISBN 1-4020-7799-8
- V.D. Castracane and M.C. Henson (eds.): Leptin. 2006. ISBN 0-387-31415-6
- G.A. Bray and D.H. Ryan (eds.): Overweight and the Metabolic Syndrome. 2006. ISBN 0-387-32163-2
- R. Azziz (ed.): The Polycystic Ovary Syndrome: Current Concepts on Pathogenesis and Clinical Care. 2007. ISBN 978-0-387-69246-3

**THE POLYCYSTIC
OVARY SYNDROME:**

**CURRENT CONCEPTS
ON PATHOGENESIS AND
CLINICAL CARE**

edited by

Ricardo Azziz, M.D., M.P.H., M.B.A.

*Chair, Dept. of Ob/Gyn, and
Director, Center for Androgen Related Disorders,
Cedars-Sinai Medical Center*

*Professor, Depts. of Ob/Gyn and Medicine
The David Geffen School of Medicine at UCLA
Los Angeles, California, USA*



Springer

Ricardo Azziz, M.D., M.P.H., M.B.A.
The Helping Hand of Los Angeles Chair in Obstetrics and Gynecology
Chair, Dept. of Ob/Gyn, and
Director, Center for Androgen Related Disorders,
Cedars-Sinai Medical Center
Professor and Vice-Chair, Dept. of Ob/Gyn, and Professor, Dept. of Medicine
The David Geffen School of Medicine at UCLA
8635 West Third Street, Suite 160W
Los Angeles, CA 90048
E-Mail: azzizr@cshs.org

THE POLYCYSTIC OVARY SYNDROME

Library of Congress Control Number: 2006939123

ISBN-13: 978-0-387-69246-3

e-ISBN-13: 978-0-387-69248-7

Printed on acid-free paper.

© 2007 Springer Science+Business Media, LLC

All rights reserved. This work may not be translated or copied in whole or in part without the written permission of the publisher (Springer Science+Business Media, LLC, 233 Spring Street, New York, NY 10013, USA), except for brief excerpts in connection with reviews or scholarly analysis. Use in connection with any form of information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed is forbidden.

The use in this publication of trade names, trademarks, service marks, and similar terms, even if they are not identified as such, is not to be taken as an expression of opinion as to whether or not they are subject to proprietary rights.

While the advice and information in this book are believed to be true and accurate at the date of going to press, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed in the United States of America.

9 8 7 6 5 4 3 2 1

springer.com

Contents

Contributors	ix
Chapter 1: Definition, Diagnosis, and Epidemiology of the Polycystic Ovary Syndrome <i>Ricardo Azziz (azzizr@cshs.org)</i>	1
1. Defining PCOS: Basics	1
2. Specific Criteria for PCOS	2
3. Diagnosis of PCOS	6
4. Prevalence of PCOS	9
5. Conclusions	11
Chapter 2: Clinical Evaluation of PCOS <i>Richard S. Legro (RSLI@psu.edu)</i>	17
1. Features of PCOS	17
2. Differential Diagnosis of PCOS	19
3. Evaluation for Insulin Resistance in PCOS	21
4. Summary	24
Chapter 3: Genetics of PCOS <i>Mark O. Goodarzi (Mark.Goodarzi@cshs.org)</i>	29
1. The Inherited Basis of PCOS and Its Component Phenotypes	29
2. The Candidate Gene Approach as Applied to PCOS Genetics	30
3. Epigenetics: A New Avenue in PCOS Genetics	39
4. Conclusions	40
Chapter 4: Insulin Action in Polycystic Ovary Syndrome: In Vivo and In Vitro <i>Jean-Patrice Baillargeon (JP.Baillargeon@usherbrooke.ca)</i>	43
1. Introduction	43
2. Insulin Action in PCOS	44
3. Androgenic Actions of Insulin in PCOS	46
4. Insulin Actions and Ovulatory Dysfunction in PCOS	54
5. Conclusions	59
6. Future Avenues of Investigation	61

Chapter 5: Ovarian Steroidogenic Abnormalities in PCOS	
<i>Jessica K. Wickenheisser and Jan M. McAllister</i> (<i>jmcallister@psu.edu</i>)	69
1. Ovarian Androgen and Estrogen Biosynthesis	70
2. Dysregulated Estrogen Biosynthesis in PCOS	72
3. Dysregulated Androgen Biosynthesis in PCOS	73
4. Increases in <i>CYP17</i> and <i>CYP11A1</i> Gene Transcription and mRNA Stability in PCOS	75
5. Insulin Sensitivity and the PCOS Ovary	77
6. Mitogen Activated Protein Kinase Signaling and Altered Steroid Biosynthesis in PCOS	77
7. Gene Expression Profiling and Candidate Gene Analysis in PCOS	78
8. Paracrine and Autocrine Regulators that May Impact Ovarian Steroid Abnormalities and Follicular Growth in the PCOS Ovary	80
9. Summary	82
Chapter 6: Role of Obesity and Adiposity in PCOS	
<i>Renato Pasquali, Laura Patton, Evanthia Diamanti-Kandarakis,</i> <i>and Alessandra Gambineri</i> (<i>renato.pasquali@unibo.it</i>)	85
1. Prevalence of Obesity in PCOS	86
2. Pattern and Implications of Body Fat Distribution in Women with PCOS	87
3. Pathophysiology of Obesity on the Hyperandrogenic, Ovulatory, and Metabolic Alterations of PCOS	88
4. Summary and Perspectives	96
Chapter 7: Strategies for Ovulation Induction in the Management of Anovulatory Polycystic Ovary Syndrome	
<i>Adam Balen</i> (<i>adam.balen@leedsth.nhs.uk</i>)	99
1. PCOS and Anovulatory Infertility: The Basics	99
2. Lifestyle and Weight Loss in PCOS	101
3. CC Therapy	102
4. Aromatase Inhibitors	104
5. Gonadotropin Therapy	104
6. Surgical Ovulation Induction	105
7. The Role of Metformin and Other Insulin Sensitizers	107
8. IVF in Women with Polycystic Ovaries	110
9. IVM of Oocytes	112
10. Summary	112

Chapter 8: Long-Term Morbidity of PCOS

Ricardo Azziz (azzizr@cshs.org)

117

1. Introduction

117

2. Prevalence of Principal Morbidities Associated with PCOS

117

3. Estimating the Economic Burden of PCOS

124

4. Conclusions

124

Index

131

Contributors

Ricardo Azziz, MD, MPH, MBA

Dept. of Ob/Gyn and Center for Androgen Related Disorders
Cedars-Sinai Medical Center
8635 West Third Street, Suite 160W
Los Angeles, CA 90048

Jean-Patrice Baillargeon, MD, MSc

Division of Endocrinology
Université de Sherbrooke
3001, 12th North Avenue
Sherbrooke, Quebec, Canada J1H 5N4

Adam Balen, MD, FRCOG

Reproductive Medicine and Surgery
Leeds General Infirmary
Leeds LS2 9NS, UK

Evanthia Diamanti-Kandarakis, MD

Endocrine Section of First Department of Internal Medicine
Athens University School of Medicine
Laiko General Hospital
Athens, Greece

Mark Goodarzi, MD, PhD

Center for Androgen Related Disorders
Cedars-Sinai Medical Center
8635 West Third Street, Suite 160W
Los Angeles, CA 90048

Alessandra Gambineri, MD

Division of Endocrinology
Department of Internal Medicine
University Alma Mater Studiorum
S. Orsola-Malpighi Hospital
Bologna, Italy

Richard S. Legro, MD

Dept of Ob/Gyn
Pennsylvania State University College of Medicine
M.S. Hershey Medical Center
500 University Drive
Hershey, PA 17033

Jan M. McAllister PhD

Department of Cellular and Molecular Physiology
Penn State Hershey College of Medicine
500 University Drive, C4723
Hershey, PA 17033

Renato Pasquali, MD

U.O. di Endocrinologia
Dipt. Medicina Interna
Azienda Policlinico S. Orsola-Malpighi
Via Massarenti 9
40138 Bologna, Italy

Laura Patton, MD

Division of Endocrinology
Department of Internal Medicine
University Alma Mater Studiorum
S. Orsola-Malpighi Hospital
Bologna, Italy

Jessica K. Wickenheisser, PhD

Departments of Cellular and Molecular Physiology
Pennsylvania State University College of Medicine
500 University Drive, C4723
Hershey, PA 17033