

# The Complete Guide to Male Fertility Preservation

Ahmad Majzoub  
Ashok Agarwal  
*Editors*

 Springer

# The Complete Guide to Male Fertility Preservation

Ahmad Majzoub • Ashok Agarwal  
Editors

# The Complete Guide to Male Fertility Preservation

 Springer

*Editors*

Ahmad Majzoub  
Department of Urology  
Hamad Medical Corporation  
Doha, Qatar

Ashok Agarwal  
Department of Urology, Andrology Center  
Cleveland Clinic  
Cleveland, OH, USA

ISBN 978-3-319-42395-1      ISBN 978-3-319-42396-8 (eBook)  
DOI 10.1007/978-3-319-42396-8

Library of Congress Control Number: 2017955680

© Springer International Publishing AG 2018

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Printed on acid-free paper

This Springer imprint is published by Springer Nature  
The registered company is Springer International Publishing AG  
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

*We dedicate our book to Young Patients with Cancer seeking fertility preservation services before treatment of their disease. It is an honor to serve these brave men.*

# Foreword



With the dramatic increase in cancer rates in reproductive-age men, the rapidly emerging understanding of the genetics of infertility, and important advances in assisted reproductive technologies, our field has been waiting for a unifying treatise on the preservation of male fertility. Drs. Majzoub and Agarwal are to be congratulated for providing a state-of-the-art guide that focuses on critical techniques for fertility preservation, from the management of ejaculatory dysfunction to the use of microsurgical techniques for refractory nonobstructive azoospermia. They address complex developing topics including the role of postmortem sperm retrieval as well as cryopreservation issues in special populations such as adolescents and transgender patients. Careful focus is placed on the technical and compliance issues of maintaining a high quality sperm bank. The book closes with an important nod to the future, reviewing potential for developments in fertility preservation including germ and stem cell transplantation as well as induction of neospermatogenesis.

This text represents a *tour de force* in the field of fertility preservation. It will be an invaluable resource for urologists, medical oncologists, andrologists, reproductive endocrinologists, pediatricians, and a myriad of other health professionals who participate in the care of men in their reproductive years. These authors deserve great praise for providing an understandable, evidence-based review of fertility preservation options. The issue of preserving the ability to conceive is of paramount importance to our patients and deserves equal attention by health care professionals.

This text represents a *tour de force* in the field of fertility preservation. It will be an invaluable resource for urologists, medical oncologists, andrologists, reproductive endocrinologists, pediatricians, and a myriad of other health professionals who participate in the care of men in their reproductive years. These authors deserve great praise for providing an understandable, evidence-based review of fertility preservation options. The issue of preserving the ability to conceive is of paramount importance to our patients and deserves equal attention by health care professionals.

Cleveland, OH, USA

Edmund Sabanegh Jr.

# Preface

Fertility preservation has witnessed major advancements in the last decade along with other aspects of male reproduction. It is considered as an essential service in medical field due to societal changes leading to delays in parenthood coupled with rapid pace of scientific discoveries propelled by technological breakthroughs in cancer treatment and cryobiology. Cancer is well accepted as a significant circumstance where fertility preservation is an essential procedure. Global demographic and epidemiologic data signal a continuous increase in cancer prevalence, with over 20 million new cancer cases expected annually by 2025. Though finding a cure remains our utmost and paramount goal, nevertheless we are faced with a challenging outcome to treatment as a growing number of patients face quality of life issues resulting from the presence of malignancy as well as the subsequent treatment. Fertility remains the leading quality of life concern in young cancer survivors. As such, the need for fertility preservation strategies is crucial now as there is an increased long-term cancer survival rate. Recent evidence indicates that the 5-year relative survival rate for all cancers combined is now approaching 70% among adults and >80% among children. The focus on fertility preservation is currently limited to cancer patients during their reproductive age, yet its clinical relevance may well be expanded to noncancer patients. Consequently, much broader applications are expected in the near future.

Our book is unique in being a complete guide to male fertility preservation. Experts from various parts of the world have contributed to make this book an important reference and an extensive guide to the multidisciplinary approach which is favored in fertility preservation. The book is divided into 4 parts. Part I provides the reader with a thoughtful and comprehensive overview of the pathophysiologic processes interrelating cancer and its treatment with infertility. It also discusses different methods of sperm preservation and fertility outcomes in cancer patients. Part II explores male fertility preservation in various noncancerous conditions such as immunosuppressed, hypogonadal, and transgender patients. The manuscript reviews in its third part the fundamental principles of cryobiology and sperm optimization and more importantly offers essential building blocks for scientists to develop a sperm banking service and implement high standards of practice. Finally, the last

part offers an understanding of the current practices of male fertility preservation along with its psychological impact on patients and extends beyond to present a glimpse of future innovative methods (tissue preservation, xenografting and artificial gametes) being implemented in this field.

We are confident that our book will be a useful guide for scientists, embryologists, and other healthcare workers practicing reproductive medicine and oncology. In addition, it will be a valuable resource for students and researchers wishing to learn more about this subject. We are highly thankful to a large number of experts who worked hard to contribute the latest, well-written and well-researched articles; without their active support, this book would not be possible. We wish to express our deep gratitude to the superb organizational and management skills of Michael D. Sova, Development Editor, and the overall support and supervision of this project by Kristopher Spring, Editor at Springer. This book is dedicated to our parents, families, mentors, and patients.

Doha, Qatar  
Cleveland, OH, USA

Ahmad Majzoub, MD  
Ashok Agarwal, PhD



# Contents

## Part I Fertility Preservation in Cancer Patients

- 1 Etiology of Cancer-Induced Male Infertility** ..... 3  
Julie Won-Ching Cheng and Edmund Y. Ko
- 2 Impact of Cancer Treatment on Sperm Chromatin Integrity** ..... 19  
Marij Dinkelman-Smit
- 3 Testicular Sperm Retrieval for Cryopreservation in Cancer Patients** ..... 33  
Gagan Prakash and Rupin Shah
- 4 Sperm Retrieval in Ejaculatory Dysfunction** ..... 43  
Mohamed Arafa, Haitham Elbardisi, and Ahmad Majzoub
- 5 The Effect of Cancer and Its Treatment on Natural-Born Offspring** ..... 57  
Zachary J. McDowell, Mark S. Hockenberry, and Larry I. Lipshultz
- 6 ART Success and Long-Term Outcomes on Offspring of Cancer Survivors** ..... 67  
Peter T.K. Chan and Maria Belén Herrero

## Part II Fertility Preservation: Special Conditions

- 7 Fertility Preservation in Adolescents with Cancer** ..... 79  
Lenore Omesi and Jennifer Levine
- 8 Testis-Sparing Surgery: Balancing Cancer Control with Fertility Preservation** ..... 93  
Muhammad A. Bulbul and Bassel G. Bachir
- 9 Fertility Preservation in Hypogonadal Men** ..... 105  
Robert J. Carrasquillo and Ranjith Ramasamy

<b>10 Sperm Preservation in Transgender Patients</b> .....	121
Chloë De Roo and Guy T'Sjoen	
<b>11 Postmortem Sperm Retrieval: Ethical, Legal, and Logistical Considerations</b> .....	129
Miriam Hadj-Moussa, Kaitlyn DelBene, Carl Cohen, Dale L. Hebert, and Dana A. Ohl	
<b>Part III Sperm Banking: Technical Issues, Standards and Maintenance</b>	
<b>12 The First Visit: Consult and Workup Before Sperm Banking</b> .....	147
Alan Scott Polackwich Jr. and Maurilio Garcia-Gil	
<b>13 Developing a Sperm Banking Consent Process</b> .....	169
Lisa Campo-Engelstein and Nanette Elster	
<b>14 The Process of Sperm Cryopreservation, Thawing and Washing Techniques</b> .....	183
Sajal Gupta, Rakesh Sharma, and Ashok Agarwal	
<b>15 Sperm Freezing Injuries</b> .....	205
Pankaj Talwar and Pranay Ghosh	
<b>16 Risk Preparedness in Sperm Banks</b> .....	227
Gary N. Clarke	
<b>17 Licensing and Accreditation of a Sperm Bank for Therapeutic Banking</b> .....	241
Michael Jurewicz and Bruce R. Gilbert	
<b>Part IV Current Practice and Future of Male Fertility Preservation</b>	
<b>18 Current Practice, Attitude, and Knowledge of Oncologists Regarding Male Fertility Preservation</b> .....	337
Jenny Riley and Sara Barnato Giordano	
<b>19 Psychological Impact and Barriers to Fertility Preservation in Male Cancer Patients</b> .....	347
Angela K. Lawson	
<b>20 Germ Cell Transplantation and Neospermatogenesis</b> .....	361
Aya Uchida and Ina Dobrinski	
<b>Index</b> .....	377

# Contributors

**Ashok Agarwal, PhD** Department of Urology, Andrology Center, Cleveland Clinic, Cleveland, OH, USA

**Mohamed Arafa, MD** Department of Urology, Hamad Medical Corporation, Doha, Qatar

**Bassel G. Bachir, MD** Division of Urology, Department of Surgery, American University of Beirut, Beirut, Lebanon

**Muhammad A. Bulbul, MD, FRCSC** Division of Urology, Department of Surgery, American University of Beirut, Beirut, Lebanon

**Lisa Campo-Engelstein, PhD** Alden March Bioethics Institute and Department of Obstetrics and Gynecology, Albany Medical College, Albany, NY, USA

**Robert J. Carrasquillo, MD** Department of Urology, University of Miami Health System, Miller School of Medicine, Miami, FL, USA

**Peter T.K. Chan, MD, CM, MSc, FRCS(C), FACS** Department of Surgery, McGill University, Montreal, QC, Canada

Department of Urology, Research Institute of the McGill University Health Center, Montreal, QC, Canada

**Julie Won-Ching Cheng, MD, MAE** Department of Urology, Loma Linda University Health, Loma Linda, CA, USA

**Gary N. Clarke, DSc** Andrology Unit, The Royal Women's Hospital, Parkville, VIC, Australia

**Carl Cohen, PhD** Residential College, University of Michigan, Ann Arbor, MI, USA

**Kaitlyn DelBene, JD** Office of the Vice-President and General Counsel, University of Michigan, Ann Arbor, MI, USA

**Chloë De Roo, MD** Department of Reproductive Medicine, Ghent University Hospital, Ghent, Belgium

**Marij Dinkelman-Smit, MD, PhD, FEBU** Department of Urology, University Medical Center, Erasmus MC, Rotterdam, The Netherlands

**Ina Dobrinski, DMV, MVSc, PhD, Dipl. ACT** Department of Comparative Biology and Experimental Medicine, University of Calgary, Calgary, AL, Canada

**Haitham Elbardisi, MD** Department of Urology, Hamad Medical Corporation, Doha, Qatar

**Nanette Elster, JD, MPH** Alden March Bioethics Institute and Department of Obstetrics and Gynecology, Albany Medical College, Albany, NY, USA

**Maurilio Garcia-Gil, MD** Department of Urology, Columbia University, Mount Sinai Medical System, Miami Beach, FL, USA

**Bruce R. Gilbert, MD, PhD** Arthur Smith Institute for Urology, Northwell Health, Lake Success, NY, USA

**Pranay Ghosh, MBBS, MS, M.Med. Sci (ART)** Department of Reproductive Medicine, Elixir Fertility Centre, New Delhi, India

**Sara Barnato Giordano, MD** Division of Hematology/Oncology, Department of Medicine, Medical University of South Carolina, Charleston, SC, USA

**Sajal Gupta, MD** Department of Urology, Andrology Center, Cleveland Clinic, Cleveland, OH, USA

**Miriam Hadj-Moussa, MD** Department of Urology, University of Michigan Health System and Medical School, Ann Arbor, MI, USA

**Dale L. Hebert, JD** Office of the Vice-President and General Counsel, University of Michigan, Ann Arbor, MI, USA

**Maria Belén Herrero, PhD** McGill University Health Center, Montreal, QC, Canada

**Mark S. Hockenberry, MD** Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA

**Michael Jurewicz, MD** Arthur Smith Institute for Urology, Northwell Health, Lake Success, NY, USA

**Edmund Y. Ko, MD** Department of Urology, Loma Linda University Health, Loma Linda, CA, USA

**Angela K. Lawson, PhD** Department of Obstetrics and Gynecology, Northwestern University, Chicago, IL, USA

**Jennifer Levine, MD, MSW** Division of Pediatric Hematology and Oncology, Weill Cornell Medicine, New York, NY, USA

**Larry I. Lipshultz, MD** Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA

**Ahmad Majzoub, MD** Department of Urology, Hamad Medical Corporation, Doha, Qatar

**Zachary J. McDowell, MD** Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA

**Dana A. Ohl, MD** Department of Urology, University of Michigan Health System and Medical School, Ann Arbor, MI, USA

**Lenore Omesi, MD** Division of Pediatric Hematology, Oncology, and Stem Cell Transplant, New York-Presbyterian Morgan Stanley Children's Hospital and Columbia University Medical Center, New York, NY, USA

**Alan Scott Polackwich Jr., MD** Department of Urology, Columbia University, Mount Sinai Medical System, Miami Beach, FL, USA

**Gagan Prakash, MS, DNB** Division Urooncology, Department of Surgical Oncology, Tata Memorial Hospital, Mumbai, Maharashtra, India

**Ranjith Ramasamy, MD** Department of Urology, University of Miami Health System, Miller School of Medicine, Miami, FL, USA

**Jenny Riley, MD** Division of Hematology/Oncology, Department of Medicine, Medical University of South Carolina, Charleston, SC, USA

**Rupin Shah, MS, MCh** Department of Urology-Andrology, Lilavati Hospital and Research Centre, Mumbai, Maharashtra, India

**Rakesh Sharma, PhD** Department of Urology, Andrology Center, Cleveland Clinic, Cleveland, OH, USA

**Guy T'Sjoen, MD, PhD** Department of Endocrinology and Center for Sexology and Gender, Ghent University Hospital, Ghent, Belgium

**Pankaj Talwar, MD, PhD** Department of Reproductive Medicine, Elixir Fertility Centre, New Delhi, India

**Aya Uchida, DVM** Department of Comparative Biology and Experimental Medicine, University of Calgary, Calgary, AL, Canada

## About the Editors



**Ashok Agarwal, PhD, HCLD (ABB), ELD (ACE)**

Ashok Agarwal is the Director of the Andrology Center and Reproductive Tissue Bank, and the Director of Research at the American Center for Reproductive Medicine since 1993. He holds these positions at the Cleveland Clinic Foundation, where he is a Professor at the Lerner College of Medicine of Case Western Reserve University and holds a Full Staff position in Urology, with secondary appointments in Ob-Gyn, Immunology, and Anatomical Pathology. Ashok received his PhD in 1983 and did his postdoctoral training in Reproductive Biology under a fellowship from the Rockefeller Foundation at

Harvard Medical School, Boston, from 1984 to 1986. He was an Instructor in Surgery and then an Assistant Professor of Urology at Harvard Medical School from 1988 to 1993. Ashok has over 25 years of experience in directing busy male infertility diagnostic facilities and fertility preservation services. He is very well published and has over 600 scientific papers and reviews in scientific journals and over 200 chapters in medical textbooks. He is ranked in Scopus as the #1 author in the world in the fields of Male Infertility/ Andrology and Human Assisted Reproduction. This recognition is based on the number of peer-reviewed publications (575), citation scores (22,640), and Hirsch index (82). He is currently an editor of 34 medical textbooks/manuals related to male infertility, ART, fertility preservation, DNA damage, and antioxidants. He is active in basic and clinical research and his laboratory has trained over 1000 scientists, clinicians, graduate and undergraduate students from the United States and abroad. His current research interests include proteomics of male infertility, molecular markers of oxidative stress, DNA integrity, apoptosis in the pathophysiology of male reproduction, and fertility preservation in patients with cancer. Ashok can be reached via email: [agarwaa@ccf.org](mailto:agarwaa@ccf.org). To learn more about Ashok or his research, visit the website of the American Center for Reproductive Medicine: <http://www.clevelandclinic.org/reproductiveresearchcenter/>; ResearchGate: [https://www.researchgate.net/profile/Ashok\\_Agarwal2](https://www.researchgate.net/profile/Ashok_Agarwal2); and Wikipedia: [https://en.wikipedia.org/wiki/Ashok\\_Agarwal](https://en.wikipedia.org/wiki/Ashok_Agarwal)



**Ahmad Majzoub, MD** is a specialist in the fields of Andrology and Male Infertility, currently holding the position of Associate Consultant in the Department of Urology at Hamad Medical Corporation, Doha, Qatar. He obtained his MBChB from Beirut Arab University in 2005 and proceeded to complete his residency training in Urology in Qatar to become an Arab Board Certified Urologist. Dr. Majzoub underwent a specialized 2-year training in Andrology and Male Infertility at the Hamad Medical Corporation and did a second Clinical and Research Fellowship in Andrology at the world-famous Glickman Urological and Kidney Institute and the American Center for Reproductive Medicine at

Cleveland Clinic Foundation, Cleveland, United States.

Dr. Majzoub provides services in General Urology, Andrology, and Male Infertility offering endoscopic, microsurgical, reconstructive, and prosthetic surgeries for his patients. His interests extend towards the management of chronic pelvic pain syndrome in men and has opened the first dedicated pelvic pain clinic in the region.

Dr. Majzoub has done extensive work in the field of Medical Research and has been very active with over 70 research publications in peer-reviewed journals and several book chapters mainly focusing on Andrology and men's health. He is a reviewer at several high impact medical journals and is an active member of the American Urological Association, the American Association for Reproductive Medicine, the European Association of Urology, the European and International Societies of Sexual Medicine, and the Arab Association of Urology. He holds editorial positions at a number of scientific journals and has had several speaker participations at national and international conferences.

Dr. Ahmad Majzoub can be reached at [dr.amajzoub@gmail.com](mailto:dr.amajzoub@gmail.com) or +(974)66676970. For more information, visit ResearchGate: [https://www.researchgate.net/profile/Ahmad\\_Majzoub](https://www.researchgate.net/profile/Ahmad_Majzoub)