Immune Infertility
Immune Infertility

The Impact of Immune Reactions on Human Infertility
Infertility is defined as the inability to conceive after having unprotected intercourse for a year. Infertility is increasing worldwide and has various causes both in the male and the female partner. Immune reactions to sperm can contribute up to 2–30% of infertility. The sperm has both autoantigenic as well as isoantigenic potential, and is thus capable of producing antisperm antibodies (ASAs) and sperm-reactive T cells in both infertile men and women. Also, over 75% vasectomized men produce autoantibodies to sperm that can cause a problem in regaining fertility even after successful re-anastomosis in vasovasostomy. Early claims regarding the incidence and involvement of ASAs in involuntary human infertility were probably overemphasized because of unreliable techniques and naivety concerning the complexity of the immune response and antigenic nature of the sperm cell. These factors, the lack of well-designed and controlled experimental studies, and the dearth of effective therapeutic modalities resulted in the confusion of the occurrence and importance of ASAs in human infertility. Consequently, evaluation of infertile couples for ASAs and their possible role in infertility was not considered a significant proposition. The development of more accurate assays and the discovery of mucosal immunity capable of responses independent of systemic immunity have caused inclusion of sperm cells and genital tract secretions in the analysis of ASAs. Furthermore, with progress in assisted reproductive and hybridoma technologies, recent developments in proteomics and genomics have tremendously increased our understanding regarding the induction and role of ASAs in infertility. It is becoming clearer now that any immunoglobulin that binds to sperm cannot be called an “antisperm antibody” unless it is directed against an antigen that is relevant to fertilization and fertility.

Although there are numerous reports on ASAs and their role in immunoinfertility, there is no book comprising various aspects of immunoinfertility under a single comprehensive treatise. This book is unique and the first of its kind in bringing together our current knowledge on immune mechanisms, proteomics, and genomics of sperm structure and function, and diagnosis and treatment of ASA-mediated infertility. Also included are chapters on the application of these immune reactions in the development of novel nonsteroidal immunoc contraceptives.

This book has 18 chapters, arranged into four sections, written by well-renowned experts in the field of immune infertility from all over the world. In Part I, various sperm antigens involved in immunoinfertility are enumerated. Chapter 1 describes the protein
structure of spermatozoa, the proteome, followed by a chapter dealing with the methods of analysis. In Chap. 2, the proteins inducing immune reactions that cause an impairment of sperm function are summarized. Section II is dedicated to the different aspects of the nature of ASAs. First, the status of immune privilege of the testis is discussed. The following chapters describe the immune chemistry of ASAs, involvement of sperm-specific T cells, the site and risk factors of ASA production, and the prevalence of ASAs in the different compartments of the body. Two other chapters on the occurrence of ASAs in women and the significance of sperm immobilizing ASAs are included. Section III addresses the clinical impact of ASAs. The chapters in this section discuss autoimmune infertility, tests for detection of sperm antibodies, impact of ASAs on male fertility and the role of assisted reproductive technologies and other methodologies to treat immunoinfertility. Section IV includes three chapters discussing the application of immune reactions to gametes and hormones in the development of novel immunocontraceptives for wildlife and humans.

In conclusion, this book is a unique and novel treatise in offering up-to-date information on ASA-mediated infertility. The authors of this book are expert investigators who are pioneers in their fields. This book will provide a model source of authentic, vital, and viable information on the latest scientific developments in the field of immunoinfertility and immunocontraception to clinicians, scientists, students, residents, and fellows working in the field of reproductive biology, obstetrics and gynecology, and urology.

Marburg, Germany
Walter K.H. Krause
Morgantown, WV, USA
Rajesh K. Naz
Contents

Section I  Sperm Antigens ........................................................................................................ 1

1.1  Proteomics of Human Spermatozoa ........................................................................ 3
    B. Nixon and R. J. Aitken

1.2  Methods of Analysis of Sperm Antigens Related to Fertility ............................. 13
    J. Shetty and J. C. Herr

1.3  Sperm Surface Proteomics ....................................................................................... 33
    B. M. Gadella

1.4  Sperm Functions Influenced by Immune Reactions .............................................. 49
    W. Krause

Section II  Antisperm Antibodies (ASA)............................................................................ 67

2.1  The Immune Privilege of the Testis ....................................................................... 69
    M. Fijak, S. Bhushan and A. Meinhardt

2.2  Immune Chemistry of ASA .................................................................................... 79
    M. Kurpisz and M. Kamieniczna

2.3  Sperm-Specific T Lymphocytes .............................................................................. 91
    W. Krause and M. Hertl

2.4  Site and Risk Factors of Antisperm Antibodies Production in the Male Population .............................................................. 97
    M. Marconi and W. Weidner

2.5  Biologic Substrates Containing ASA ..................................................................... 111
    W. Krause
2.6 ASA in the Female ................................................................. 121
   G. N. Clarke

2.7 Sperm–Immobilizing Antibody and Its Target Antigen (CD52) ................. 131
   A. Hasegawa and K. Koyama

Section III  The Clinical Impact of Sperm Antibodies ........................................ 143

3.1 Male Autoimmune Infertility ........................................................................ 145
   F. Francavilla and A. Barbonetti

3.2 Tests for Sperm Antibodies ......................................................................... 155
   A. Agarwal and T. M. Said

3.3 Impact on Fertility Outcome ...................................................................... 165
   Z. Ulcova-Gallova

3.4 Sperm Antibodies and Assisted Reproduction ............................................ 175
   J. H. Check

3.5 Treatment of Immune Infertility ................................................................. 185
   R. K. Naz

Section IV  Immune Contraception ..................................................................... 195

4.1 Immunization with Sperm Antigens to Induce Contraception..................... 197
   R. K. Naz

4.2 Immunocontraception in Wildlife Animals .................................................. 209
   K. Jewgenow

4.3 Experience from Clinical Trials with Fertility Control Vaccines ............... 223
   G. P. Talwar, S. Purswani, J. C. Gupta, and H. K. Vyas

Subject Index .................................................................................................. 233
Contributors

A. Agarwal
Cleveland Clinic Lerner College of Medicine and Case Western Reserve University, 9500 Euclid Avenue, Cleveland, OH 44195, USA
agarwaa@ccf.org

John R. Aitken
ARC Centre of Excellence in Biotechnology and Development, School of Environmental and Life Sciences, University of Newcastle Callaghan, NSW 2308, Australia
john.aitken@newcastle.edu.au

Arcangelo Barbonetti
Department of Internal Medicine, Andrologic Unit, University of L’Aquila, Coppito, 67100 L’Aquila, Italy
arcangelobarbonetti@virgilio.it

Sudhanshu Bhushan
Department of Anatomy and Cell Biology, Justus-Liebig-University of Giessen, 35385 Giessen, Germany;
sudhanshu.bhushan@anatomie.med.uni-giessen.de

Jerome H. Check
Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden, Cooper Hospital/University Medical Center, Camden, NJ, USA
laurie@ccivf.com

Gary N. Clarke
Department of Obstetrics and Gynecology, University of Melbourne Andrology Unit, Royal Women’s Hospital, Melbourne, Australia
gary.clarke@thewomens.org.au

Monika Fijak
Department of Anatomy and Cell Biology, Justus-Liebig-University of Giessen, 35385 Giessen, Germany
monika.fijak@anatomie.med.uni-giessen.de
Felice Francavilla
Department of Internal Medicine, Andrologic Unit, University of L’Aquila, Coppito, 67100 L’Aquila, Italy
francavi@cc.univaq.it

B.M. Gadella
Departments of Biochemistry and Cell Biology and of Farm Animal Health, Utrecht University, 3584 CM Utrecht, The Netherlands
B.M.Gadella@uu.nl

Jagdish Chandra Gupta
Talwar Research Foundation, E-8 Neb Valley, Neb Sarai, New Delhi-110068, India
jagdishgupta2@gmail.com

Akiko Hasegawa
Laboratory of Developmental Biology and Reproduction, Advanced Medical Sciences, Hyogo College of Medicine, Japan
zonenapel@hyo-med.ac.jp

John C. Herr
Health Science Center, University of Virginia, Charlottesville, VA 22908, USA
jch7k@virginia.edu

Michael Hertl
Department of Dermatology and Allergology, Philipp University, 35033 Marburg, Germany
hertl@med.uni-marburg.de

Katarina Jewgenow
Leibniz Institute for Zoo and Wildlife Research, PF 601103, 10252 Berlin, Germany
jewgenow@izw-berlin.de

Marzena Kamieniczna
Department of Reproductive Biology and Stem Cells, Institute of Human Genetics, Polish Academy of Sciences, Strzeszynska 32, 60-479 Poznan, Poland
kaspmarz@man.poznan.pl

Koji Koyama
Department of Obstetrics and Gynecology, Institute for Advanced Medical Sciences, Hyogo College of Medicine, 1-1 Mukogawa-cho, Nishinomiya, Hyogo 6638501, Japan
kkoyama@hyo-med.ac.jp

Walter K. H. Krause
Klinik für Dermatologie und Allergologie, Philipps-Universität, 35033 Marburg, Germany
krause@med.uni-marburg.de

Maciej Kurpisz
Department of Reproductive Biology and Stem Cells, Institute of Human Genetics, Polish Academy of Sciences, Strzeszyńska 32, 60-479 Poznan, Poland
kurpimac@man.poznan.pl

M. Marconi
Department of Urology, University of Chile, Santos Dumont 999, Santiago, Chile
marcelomarconi@yahoo.es

Andrea Meinhardt
Department of Anatomy and Cell Biology, Justus-Liebig-University of Giessen, 35385 Giessen, Germany
andreas.meinhardt@anatomie.med.uni-giessen.de
Rajesh K. Naz  
Center for Research in Reproductive Sciences (CRRS), West Virginia University, School of Medicine, 2085 Robert C. Byrd Health Sciences Center North, Morgantown, WV 26506, USA  
Rnaz@hsc.wvu.edu

Rajesh K. Naz  
Center for Research in Reproductive Sciences (CRRS), West Virginia University, School of Medicine, 2085 Robert C. Byrd Health Sciences Center North, Morgantown, WV 26506, USA  
Rnaz@hsc.wvu.edu

Brett Nixon  
School of Environmental and Life Sciences, University of Newcastle, University Drive, Callaghan, NSW 2308, Australia  
brett.nixon@newcastle.edu.au

Brett Nixon  
School of Environmental and Life Sciences, University of Newcastle, University Drive, Callaghan, NSW 2308, Australia  
brett.nixon@newcastle.edu.au

Shilpi Purswani  
Talwar Research Foundation, E-8 Neb Valley, Neb Sarai, New Delhi-110068, India  
dushtkt@gmail.com

Shilpi Purswani  
Talwar Research Foundation, E-8 Neb Valley, Neb Sarai, New Delhi-110068, India  
dushtkt@gmail.com

T.M. Said  
Andrology Laboratory and Reproductive Tissue Bank, The Toronto Institute for Reproductive Medicine, ReproMed 56 Aberfoyle Crescent, Toronto, ON M8X2W4, Canada  
tsaid@reпромed.ca

T.M. Said  
Andrology Laboratory and Reproductive Tissue Bank, The Toronto Institute for Reproductive Medicine, ReproMed 56 Aberfoyle Crescent, Toronto, ON M8X2W4, Canada  
tsaid@reпромed.ca

Jagathpala Shetty  
Center for Research in Contraceptive and Reproductive Health, University of Virginia Health Science Center, Charlottesville, VA 22908, USA  
Js4ed@virginia.edu

Jagathpala Shetty  
Center for Research in Contraceptive and Reproductive Health, University of Virginia Health Science Center, Charlottesville, VA 22908, USA  
Js4ed@virginia.edu

G.P. Talwar  
Talwar Research Foundation, E-8 Neb Valley, Neb Sarai, New Delhi-110068, India  
gptalwar@gmail.com

G.P. Talwar  
Talwar Research Foundation, E-8 Neb Valley, Neb Sarai, New Delhi-110068, India  
gptalwar@gmail.com

Z. Ulcová-Gallová  
Department of Obstetrics and Gynecology, Charles University, Alej Svobody 80, Plzen-Lochotin, 326 00, Czech Republic  
ulcova@fnplzen.cz

Z. Ulcová-Gallová  
Department of Obstetrics and Gynecology, Charles University, Alej Svobody 80, Plzen-Lochotin, 326 00, Czech Republic  
ulcova@fnplzen.cz

Hemant Kumar Vyas  
Talwar Research Foundation, E-8 Neb Valley, Neb Sarai, New Delhi-110068, India  
hemantkvyas@gmail.com

Hemant Kumar Vyas  
Talwar Research Foundation, E-8 Neb Valley, Neb Sarai, New Delhi-110068, India  
hemantkvyas@gmail.com

Wolfgang Weidner  
Department of Urology and Pediatric Urology, University Hospital Giessen and Marburg GmbH, Justus-Liebig-Universität, Rudolf- Buchheim-Street 7, 35385 Gießen, Germany  
W.weidner@chiru.med.uni-giessen.de

Wolfgang Weidner  
Department of Urology and Pediatric Urology, University Hospital Giessen and Marburg GmbH, Justus-Liebig-Universität, Rudolf- Buchheim-Street 7, 35385 Gießen, Germany  
W.weidner@chiru.med.uni-giessen.de