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Preface: Male Infertility: Is It the Key to the Future of Reproductive Health? xiii

James M. Hotaling

Cutting-Edge Evaluation of Male Infertility 129

Ujval Ishu Pathak, Joseph Scott Gabrielsen, and Larry I. Lipshultz

A male factor is a contributor in 50% of cases of infertility. Although assisted reproductive techniques can often bypass the need to improve semen parameters, the evaluation of the infertile man remains critical. Current methods for evaluating the infertile man are discussed, beginning with the basic workup that all suspected infertile men should undergo, followed by subsequent evaluation steps. Although the fundamental components of the evaluation have remained consistent, several new tools are available to assist in identifying the underlying etiology. As our understanding of male fertility expands, the technologies available to diagnose and ultimately treat it continue to evolve.

Optimal Endocrine Evaluation and Treatment of Male Infertility 139

Sarah C. McGriff, Eric M. Lo, James M. Hotaling, and Alexander W. Pastuszak

This article aims to define the optimal endocrine workup of male factor infertility, including evaluation and treatment of men who have previously been on exogenous testosterone or anabolic steroids. Future directions include the expansion of genetic testing for infertility to include endocrine gene products.

Sperm Extraction in Obstructive Azoospermia: What's Next? 147

Jason P. Akerman, Solomon Hayon, and Robert Matthew Coward

For men with obstructive azoospermia, several surgical sperm retrieval techniques can facilitate conception with assisted reproductive technology. The evolution of both percutaneous and open approaches to sperm retrieval has been affected by technological innovations, including the surgical microscope, in vitro fertilization, and intracytoplasmic sperm injection. Further modifications to these procedures are designed to minimize patient morbidity and increase the quality and quantity of sperm samples. Innovative technologies promise to further ameliorate outcomes by selecting the highest quality sperm. Although various approaches to surgical sperm retrieval are now well established, several advancements in sperm selection and optimization are being developed.

Testicular Mapping: A Roadmap to Sperm Retrieval in Nonobstructive Azoospermia? 157

Akash A. Kapadia and Thomas J. Walsh

Guiding a couple with nonobstructive azoospermia requires an integrated approach to care by the urologist and the reproductive endocrinologist. After informing the couple of the implications of the diagnosis, care must be taken to outline the options of parenthood. Most experts agree that sperm retrieval in men can be challenging. This article describes various options of sperm retrieval,

historic and contemporary, and highlights the advantages and disadvantages of each. The authors find that using a testicular map can invariably help guide sperm retrieval and overall fertility care. The right approach is one that involves a shared decision with the couple.

High Sperm DNA Damage: Does Testicular Sperm Make Sense? 165

Keith Jarvi

Sperm DNA damage reduces pregnancy rates in couples undergoing in vitro fertilization (IVF). Because it has been shown that testicular sperm have lower DNA damage than ejaculated sperm, it is an attractive idea to consider using testicular sperm for IVF for men with high sperm DNA damage. In fact, there are multiple centers throughout the world now offering sperm retrieval for IVF to manage this condition. However, there is insufficient evidence to conclude that testicular sperm improves pregnancy/live birth rates. Further studies are required before offering sperm retrieval as a standard of care to manage high sperm DNA damage.

Round Spermatid Injection 175

Kelli X. Gross, Brent M. Hanson, and James M. Hotaling

From a fertility perspective, men with azoospermia represent a challenging patient population. When no mature spermatozoa are obtained during a testicular sperm extraction, patients are often left with limited options, such as adoption or the use of donor sperm. However, it has been reported that round spermatids can be successfully injected into human oocytes and used as an alternative to mature spermatozoa. This technique is known as round spermatid injection (ROSI). Despite the limitations of ROSI and diminished clinical success rates, the use of round spermatids for fertilization may have potential as a treatment modality for men with azoospermia.

The Role of the Urologist in a Reproductive Endocrinology and Infertility Practice 185

Philip J. Cheng and Cigdem Tanrikut

With male factor infertility accounting for up to 50% of infertility cases, demand for male fertility services has increased. Integrating a reproductive urologist within a fertility center allows for treatment of both partners simultaneously with easier, more convenient access to a comprehensive male evaluation and any indicated interventions. A joint practice allows urologists to collaborate more closely with reproductive endocrinologists, which can, in turn, improve clinical care and research endeavors. This full-service, streamlined approach translates to optimized care for the infertile couple and allows for emphasis of male partner health.

Care Delivery for Male Infertility: The Present and Future 193

Mary Oakley Strasser and James M. Dupree

Although infertility is now recognized as a disease by multiple organizations including the World Health Organization and the American Medical Association, private insurance companies rarely include coverage for infertility treatments. In this review, the authors assess the current state of care delivery for male infertility care in the United States. They discuss the scope of male infertility as well as the unique burdens it places on patients and review emerging market forces that could affect the future of care delivery for male infertility.

Qualitative Research in Male Infertility 205

Akanksha Mehta

Qualitative research methods represent a valuable tool for investigating the entirety of the experience of male infertility evaluation, diagnosis, and treatment. Qualitative research is rigorous and thorough and well adapted for studying the complex field of infertility and reproductive health. Knowledge gained from qualitative research methods can undoubtedly inform clinical practice and improve support for individuals and couples affected by male factor infertility.

Male Infertility and Somatic Health 211

Mujalli Mhailan Murshidi, Jeremy T. Choy, and Michael L. Eisenberg

Somatic health is associated with male infertility; potential links between infertility and health may arise from genetic, developmental, and lifestyle factors. Studies have explored possible connections between male infertility and oncologic, cardiovascular, metabolic, chronic, and autoimmune diseases. Male infertility also may be a predictor of hospitalization and mortality. Additional research is required to elucidate the mechanisms by which male infertility affects overall health.

Transgenerational Epigenetics: A Window into Paternal Health Influences on Offspring 219

Mathew M. Grover and Timothy G. Jenkins

Transgenerational epigenetic inheritance provides a mechanism by which environmental exposures and lifestyle decisions can affect the offspring directly through the gamete. It is this pattern of inheritance that has shed light on the fact that preconception lifestyle decisions that a father makes are significant because they can significantly impact the offspring. Understanding the epigenetic alterations in gametes and the potential implications of these changes is key to the health of future generations.

Spermatogonial Stem Cell Culture in Oncofertility 227

Sherin David and Kyle E. Orwig

Infertility caused by chemotherapy or radiation treatments negatively impacts patient-survivor quality of life. The only fertility preservation option available to prepubertal boys who are not making sperm is cryopreservation of testicular tissues that contain spermatogonial stem cells (SSCs) with potential to produce sperm and/or restore fertility. SSC transplantation to regenerate spermatogenesis in infertile adult survivors of childhood cancers is a mature technology. However, the number of SSCs obtained in a biopsy of a prepubertal testis may be small. Therefore, methods to expand SSC numbers in culture before transplantation are needed. Here we review progress with human SSC culture.

Personalized Medicine in Infertile Men 245

Nicolás Garrido and Irene Hervás

Personalized medicine gathers the most relevant data involved in human health. Currently, the diagnosis of male infertility is limited to spermiogram, which does not provide information on the male fertile potential. New diagnostic methods are required. The application of omics techniques in the study of male reproductive health renders a huge amount of data providing numerous novel infertility

biomarkers, from genes to metabolites, to diagnose the cause of male infertility. Recent studies hold the promise that these biomarkers will allow a noninvasive infertility diagnosis and the improvement of the sperm selection techniques.

Male Infertility and the Future of In Vitro Fertilization

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Brent M. Hanson, Daniel J. Kaser, and Jason M. Franasiak

The male contribution to infertility has traditionally been overlooked, or at best oversimplified. In recent years efforts have been made to optimize diagnostic and therapeutic techniques to maximize fertility outcomes. A renewed focus on the male partner has resulted in an increased understanding of both genetic and epigenetic changes within the male germline. Furthermore, single-nucleotide polymorphisms, copy-number variants, DNA damage, sperm cryopreservation, obesity, and paternal age have recently been recognized as important factors that play a role in male fertility. Developing a deeper knowledge of these issues could potentially lead to improved success with assisted reproductive technology.