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# Foreword

The fifth edition of *Infertility in the Male* continues to be the gold standard in the field of infertility urology. The editors represent three generations of pioneers and leaders in the field. Within the text, each has brought their own editorial skills and writing acumen. This classic is up-to-date, as in the past. This is a rapidly changing field stimulated by the introduction to society of in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), and microsurgical epididymal sperm aspiration (MESA). Forty years ago, infertility in the male was a sleepy, not very interesting pursuit. Today it is exploding with new information, cures, and insights. As in many fields, genetics has had a profound effect. Surgical procedures, as well as basic science research, has changed hyperbolically.

Assembled authors is the who's who in the field of urology. It includes basic scientists, translational scientists, and super clinicians. The 31 chapters cover all imaginable topics. The book serves as a manual for the novice and a reference source for the experienced practitioner, as well as a well-organized convenient source of information when information desired on a single topic is wanted.

The opening shot over the bow, by the editors, entitled "why do we care for the male" gives an overview philosophical approach, as well as a historical perspective for treating male infertility.

The text is interestingly divided into anatomy, both microscopic and gross, physiology, diagnosis and workup, including the female, and therapeutic modalities.

Highlights include genomics and epigenomics of male reproduction, the environment and male infertility, and cryopreservation of sperm, including in prepubescent males.

Practical contributions include surgical sperm extraction, oncofertility, and contraception. Examples of how this text has grown and kept up with the times include chapters on inheritance of male infertility, advanced diagnostic approaches to male infertility, and future directions.

The book is beautifully illustrated and there is a uniformity in the style of writing that makes it easy to read and comprehend the content.

I quote from the fourth edition's Foreword:

> "This fourth edition of *Infertility in the Male* certainly disproves the call to arms of the reproductive medicine community: when, in 1992, ICSI (intracytoplasmic sperm injection) appeared in the armamentarium of the infertility physicians it was claimed that urologists no longer had a role in the management of infertile men, except for obtaining sperm. This concept is certainly refuted and defeated by this exquisite revision of a book whose first edition was published in 1983."

The growth in each edition is immeasurable and certainly this is true of the fifth edition of *Infertility in the Male*.

In summary, the list of contributors and editors are those who pioneered the field, illustrating the dedication and prescience in treating the infertile couple. It is clear male factor infertility has come into its own as a serious discipline.

***Alan H. DeCherney MD***

# Abbreviations

| | |
|---|---|
| **3β-HSD** | 3β-hydroxysteroid dehydrogenase |
| **11β-MNTDC** | 11β-methyl-nortestosterone-dodecylcarbonate |
| **17OHD** | 17α-hydroxylase deficiency |
| **AATB** | American Association of Tissue Banks |
| **ABA** | American Bar Association |
| **aCGH** | array comparative genomic hybridization |
| **ACOG** | American College of Obstetricians and Gynecologists |
| **ActRII** | activin receptor type II |
| **AFC** | antral follicle count |
| **AGD** | abnormal anogenital distance |
| **AGI** | anogenital index |
| **AI** | artificial intelligence |
| **AID** | artificial insemination with donor semen |
| **AIDS** | acquired immune deficiency syndrome |
| **AIS** | androgen insensitivity syndrome |
| **AJ** | adherens junction |
| **AMA** | advanced maternal age |
| **AMD** | adjusted mean difference |
| **AMH** | anti-Müllerian hormone |
| **AO** | acridine orange |
| **aPKC** | atypical protein kinase C |
| **AR** | androgen receptor |
| **AR** | acrosome reaction |
| **ARC** | arcuate nucleus |
| **ARIC** | acrosome reaction to ionophore challenge |
| **ART** | assisted reproductive technology |
| **ASA** | antisperm antibodies |
| **ASCO** | American Society of Clinical Oncology |
| **ASD** | anoscrotal distance |
| **ASRM** | American Society for Reproductive Medicine |
| **ATP** | adenosine triphosphate |
| **AUA** | American Urological Association |
| **AZF** | azoospermia factor |
| **AZFa** | azoospermia factor a |
| **AZFb** | azoospermia factor b |
| **AZFc** | azoospermia factor c |
| **AZT** | zidovudine |
| **BBT** | basal body temperature |
| **BCG** | bacille Calmette–Guérin |
| **BEB** | blood–epididymis barrier |
| **BMI** | body mass index |
| **BN** | Brown Norway |
| **BPA** | bisphenol A |
| **BPH** | benign prostate hyperplasia |
| **BRDT** | bromodomain testis-associated |
| **BrdU** | bromodeoxyuridine |
| **BTB** | blood–testis barrier |
| **cAMP** | cyclic adenosine monophosphate |
| **Cas9** | CRISPR-associated protein 9 |
| **CASA** | computer-assisted semen analysis |
| **CatSper** | cation channels of sperm |
| **CBAVD** | congenital bilateral absence of the vas deferens |
| **CBP** | chronic bacterial prostatitis |
| **CBRC** | cross-border reproductive care |
| **CBS** | Cryo Bio System |
| **CDC** | Centers for Disease Control and Prevention |
| **cDNA** | complementary DNA |
| **CDUS** | color Doppler ultrasound |
| **CF** | cystic fibrosis |
| **CFTR** | cystic fibrosis transmembrane conductance regulator |
| **cGMP** | cyclic guanosine monophosphate |
| **CI** | confidence interval |
| **CL** | chemiluminescence |
| **CLIA** | Clinical Laboratory Improvement Amendment |
| **CMS** | Centers for Medicare and Medicaid Services |
| **CMV** | cytomegalovirus |
| **CNS** | central nervous system |
| **CNV** | copy number variation |
| **CoQ10** | coenzyme Q10 |
| **COSMIC** | Catalogue of Somatic Mutations in Cancer |
| **COX** | cyclooxygenase |
| **COX-1** | cyclooxygenase 1 |
| **COX-2** | cyclooxygenase 2 |
| **CP** | chronic prostatitis |
| **CPA** | cyproterone acetate |
| **CpG** | cytosine phosphate guanine |
| **CPPS** | chronic pelvic pain syndrome |
| **Crb3** | Crumbs homolog-3 |
| **CREB** | cAMP response element binding protein |
| **CRISPR** | clustered regularly interspaced short palindromic repeats |
| **CT** | computed tomography |
| **CUA** | Canadian Urological Association |
| **CUAVD** | congenital unilateral absence of the vas deferens |
| **DAPI** | 4′,6-diamidino-2-phenylindole |
| ***DAZ*** | Deleted in Azoospermia |

| | |
|---|---|
| **DBCP** | 1,2-dibromo-3-chloropropane |
| **DBD** | DNA-binding domain |
| **DBD-FISH** | DNA breakage detection-fluorescence *in situ* hybridization |
| **DC** | dendritic cell |
| **DDT** | dichlorodiphenyltrichloroethane |
| **DEHP** | di-ethyl-hexyl phthalate |
| **DES** | diethylstilbestrol |
| **DFI** | DNA fragmentation index |
| **DFS** | dysplasia of the fibrous sheath |
| **DHEA** | dehydroepiandrosterone |
| **DHEAS** | dehydroepiandrosterone sulfate |
| **DHT** | dihydrotestosterone |
| **DI** | donor insemination |
| **Dlg1** | discs large 1 |
| **DMAU** | dimethandrolone undecanoate |
| **DMSO** | dimethyl sulfoxide |
| **DNMT** | DNA methyl transferase |
| **DOR** | diminished ovarian reserve |
| **dpp** | days postpartum |
| **DSB** | DNA strand break |
| **DSD** | disorder of sex development |
| **dsDNA** | double-stranded DNA |
| **DSM-5** | *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition |
| **dUTP** | deoxyuridine triphosphate |
| **Dvl3** | Disheveled 3 |
| **EAU** | European Association of Urology |
| **EB** | elementary body |
| **EBV** | Epstein–Barr virus |
| **ED** | erectile dysfunction |
| **EDC** | endocrine disrupting chemical |
| **EDO** | ejaculatory duct obstruction |
| **EEJ** | electroejaculation |
| **EGR1** | early growth response 1 |
| **ELISA** | enzyme-linked immunosorbent assay |
| **EOP** | endogenous opioid peptide |
| **EPA** | Environmental Protection Agency |
| **EPPIN** | epididymal protease inhibitor |
| **EPS** | expressed prostatic secretions |
| **ER** | estrogen receptor |
| **ERKO** | estrogen receptor-α knockout |
| **ES** | ectoplasmic specialization |
| **ESHRE** | European Society of Human Reproduction and Embryology |
| **ESR** | estrogen receptor |
| **ESUR-SPIQG** | European Society of Urogenital Radiology Scrotal and Penile Imaging Working Group |
| **EV** | epididymovasostomy |
| **EST** | Estrogen Therapy |
| **FDA** | Food and Drug Administration |
| **FHA** | functional hypothalamic amenorrhea |
| **FIGO** | International Federation of Gynecology and Obstetrics (FIGO) |
| **FISH** | fluorescence *in situ* hybridization |
| **FLCIVF** | Friends of the Low-Cost Ivf Foundation |
| **Fmi** | Flamingo |
| **FNA** | fine needle aspiration |
| **FOAD** | fetal origins of adult disease |
| **FP** | fertility preservation |
| **Fr** | French |
| **FSH** | follicle-stimulating hormone |
| **FSHR** | follicle-stimulating hormone receptor |
| **Fzd** | Frizzled |
| **G** | gauge |
| **GABA** | gamma aminobutyric acid |
| **GalNAc** | N-acetylgalactosamine |
| **GAPDHS** | sperm-specific glyceraldehyde-3-phosphate dehydrogenase |
| **GAPDS** | sperm-specific glyceraldehyde-3-phosphate dehydrogenase |
| **GAS** | gender-affirming surgery |
| **GGT** | γ-glutamyltranspeptidase |
| **GlcNAc** | N-acetylglucosamine |
| **GnRH** | gonadotropin-releasing hormone |
| **GnRHR** | gonadotropin-releasing hormone receptor |
| **GPI** | glycosyl phosphatidylinositol |
| **GTP** | guanosine triphosphate |
| **GU** | genitourinary |
| **GWAS** | genome-wide association studies |
| **HA** | hyperactivated |
| **HA** | hyaluronic acid |
| **HAART** | highly active antiretroviral therapy |
| **hCG** | human chorionic gonadotropin |
| **HDM** | histone demethylase |
| **HEPES** | N-hydroxyethylpiperazine-N-ethanesulfonate |
| **HEX-B** | hexosaminidase type B |
| **HHV** | human herpesvirus |
| **HIF-1α** | hypoxia-inducible factor 1 alpha |
| **HIV** | human immunodeficiency virus |
| **hMG** | human menopausal gonadotropin |
| **HOS** | hypo-osmotic swelling |
| **HPA** | hypothalamic–pituitary–adrenal |
| **HPF** | high-powered field |
| **HPG** | hypothalamic–pituitary–gonadal |
| **HPO** | hypothalamic–pituitary–ovarian |
| **HPT** | hypothalamic–pituitary–testicular |
| **HPV** | human papillomavirus |
| **HR** | hazard ratio |
| **HSA** | human serum albumin |
| **HSG** | hysterosalpingography |
| **HSP** | heat shock protein |
| **HSP60** | 60-kDa heat shock protein |
| **HSV** | herpes simplex virus |
| **HTF** | human tubal fluid |
| **HTLV** | human T-cell leukemia virus |
| **HyCoSy** | hysterosalpingo-contrast sonography |
| **HZA** | hemizona assay |
| **HZI** | hemizona index |
| **ICSI** | intracytoplasmic sperm injection |
| **IDO** | indoleamine 2,3-dioxygenase |
| **IFFS** | International Federation of Fertility Societies |
| **IFRR** | Infertility Family Research Registry |

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|---|---|
| **IGD** | isolated gonadotropin-releasing hormone deficiency |
| **IGF** | insulin-like growth factor |
| **IHH** | idiopathic/isolated hypogonadotropic hypogonadism |
| **IIEF** | International Index of Erectile Function |
| **IL** | interleukin |
| **IM** | intramuscularly |
| **IMG** | inferior mesenteric ganglia |
| **IMSI** | intracytoplasmic morphologically selected sperm injection |
| **INSL3** | insulin-like factor 3 |
| **IP** | intraperitoneal |
| **ISBER** | International Society for Biological and Environmental Repositories |
| **IUD** | intrauterine device |
| **IUI** | intrauterine insemination |
| **IVC** | inferior vena cava |
| **IVF** | in vitro fertilization |
| **KD** | knockdown |
| **KNDy** | kisspeptin/neurokinin B/dynorphin |
| **KS** | Klinefelter syndrome |
| **KSper** | sperm-specific potassium |
| **LBD** | ligand binding domain |
| **LCIVF** | low-cost in vitro fertilization |
| **LCR** | ligase chain reaction |
| **Lgl2** | lethal giant larvae 2 |
| **LH** | luteinizing hormone |
| **LHRH** | luteinizing hormone-releasing hormone |
| **lncRNA** | long noncoding RNA |
| **LNG** | levonorgestrel |
| **LPO** | lipid peroxidation |
| **LPS** | lipopolysaccharide |
| **MA** | maturation arrest |
| **mAb** | monoclonal antibodies |
| **MACS** | magnetic-activated cell sorting |
| **MAIS** | mild androgen insensitivity syndrome |
| **MAOI** | monoamine oxidase inhibitor |
| **MAP** | microtubule affinity protein |
| **MAPK** | mitogen-activated protein kinase |
| **MAR** | medically assisted reproduction |
| **MAR** | mixed agglutination reaction |
| **MCAF** | monocyte chemotactic and activating factor |
| **MER** | monocyte-to-eosinophil ratio |
| **MESA** | microsurgical epididymal sperm aspiration |
| **MGI** | Mouse Genome Informatics |
| **MHC** | major histocompatibility complex |
| **microTESE** | microscopic/microdissection testicular sperm extraction |
| **miRNA** | microRNA |
| **MIV** | minimally invasive vasectomy |
| **MMAF** | multiple morphologic abnormalities of the sperm flagella |
| **MMAS** | Massachusetts Male Aging Study |
| **MMP2** | matrix metalloprotease 2 |
| **MMP9** | matrix metalloprotease 9 |
| **MPOA** | medial preoptic area |
| **MRI** | magnetic resonance imaging |
| **MRKH** | Mayer–Rokitansky–Küster–Haus syndrome |
| **MSDS** | material safety data sheet |
| **MT** | microtubule |
| **mTESE** | microdissection testicular sperm extraction |
| **mV** | millivolt |
| **Mwh** | Multiple wing hairs |
| **NBP** | nonbacterial prostatitis |
| **ncRNA** | noncoding RNA |
| **NES** | nestorone |
| **NHE** | sodium–hydrogen exchanger |
| **NHL** | non-Hodgkin's lymphoma |
| **NHS** | Nance–Horan syndrome |
| **NIEHS** | National Institute of Environmental Health Sciences |
| **NIH** | National Institutes of Health |
| **NIOSH** | National Institute for Occupational Safety and Health |
| **NKB** | neurokinin B |
| **NLR** | neutrophil-to-lymphocyte ratio |
| **NNRTI** | non-nucleoside reverse transcriptase inhibitor |
| **NO** | nitric oxide |
| **NOS** | nitric oxide synthase |
| **NPY** | neuropeptide Y |
| **NSAID** | nonsteroidal anti-inflammatory drug |
| **NSV** | no-scalpel vasectomy |
| **OA** | obstructive azoospermia |
| **OAT** | oligoasthenoteratospermia |
| **OI** | obstructive interval |
| **OMIM** | Online Mendelian Inheritance in Man |
| **OSHA** | Occupational Safety and Health Administration |
| **PAH** | polycyclic aromatic hydrocarbon |
| **PAIS** | partial androgen insensitivity syndrome |
| **PAR** | pseudoautosomal region |
| **PAS** | periodic acid–Schiff |
| **PatJ** | Pals1-associated tight junction protein |
| **PBZ** | phenoxybenzamide |
| **PCB** | polychlorinated biphenyl |
| **PCD** | primary ciliary dyskinesia |
| **PCOS** | polycystic ovary syndrome |
| **PCP** | planar cell polarity |
| **PCR** | polymerase chain reaction |
| **PCT** | postcoital test |
| **Pd** | prostatodynia |
| **PDE** | phosphodiesterase |
| **PDE5** | phosphodiesterase type 5 |
| **PDE5-I** | phosphodiesterase type 5 isoform inhibitor |
| **PDGF** | platelet-derived growth factor |
| **PESA** | percutaneous epididymal sperm aspiration |
| **PETG** | polyethylene terephthalate |
| **PEU** | postejaculatory urinalysis |
| **PGC** | primordial germ cell |
| **PGCN** | paragigantocellular nucleus |
| **PID** | pelvic inflammatory disease |
| **piRNA** | Piwi-interacting RNA |

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|---|---|
| **PITX1** | paired-like homeodomain transcription factor 1 |
| **PKA** | protein kinase A |
| **PKC** | protein kinase C |
| **PLCζ** | phospholipase C zeta |
| **PLR** | platelet-to-lymphocyte ratio |
| **POI** | primary ovarian insufficiency |
| **PPV** | positive predictive value |
| **PSA** | prostate-specific antigen |
| **PTEN** | phosphatase and tensin homolog |
| **PVC** | polyvinyl chloride |
| **PVE** | prostatovesiculoepididymitis |
| **PVN** | paraventricular nucleus |
| **PVS** | penile vibratory stimulation |
| **PVSA** | postvasectomy semen analysis |
| **RB** | reticulate body |
| **RCT** | randomized controlled trial |
| **rFSH** | recombinant FSH |
| **rhFSH** | recombinant human FSH |
| **rhLH** | recombinant human LH |
| **RI** | resistive index |
| **RISUG** | reversible inhibition of sperm under guidance |
| **RNAi** | RNA interference |
| **RNMS** | rare nonmotile sperm |
| **RNS** | reactive nitrogen species |
| **ROK** | Rho-associated kinase |
| **ROS** | reactive oxygen species |
| **RT-PCR** | reverse transcriptase polymerase chain reaction |
| **RXFP2** | relaxin family peptide receptor 2 |
| **SARM** | selective androgen receptor modulator |
| **SART** | Society for Assisted Reproductive Technology |
| **SAS** | sympathetic–adrenal system |
| **SC** | subcutaneously |
| **SCD** | sperm chromatin dispersion |
| **SCI** | spinal cord injury |
| **SCO** | Sertoli cell-only |
| **SCSA®** | Sperm Chromatin Structure Assay |
| **SDF** | sperm DNA fragmentation |
| **SEMG1** | semenogelin 1 |
| **SERM** | selective estrogen receptor modulator |
| **SF1** | steroidogenic factor 1 |
| **SGE** | spinal generator for ejaculation |
| **SHBG** | sex hormone-binding globulin |
| **SHIM** | Sexual Health Inventory for Men |
| **SHOX** | short homeobox gene affecting stature |
| **shRNA** | short hairpin RNA |
| **siRNA** | small interfering ribonucleic acid |
| **SIS** | saline infusion sonohysterography |
| **sncRNA** | small noncoding RNA |
| **sNHE** | sperm-specific sodium–hydrogen exchanger |
| **SNP** | single nucleotide polymorphism |
| **SNRI** | serotonin norepinephrine reuptake inhibitor |
| **SPA** | sperm penetration assay |
| **spp.** | species |
| **SRR** | sperm retrieval rate |
| **SSC** | spermatogonial stem cell |
| **ssDNA** | single-stranded DNA |
| **SSRI** | selective serotonin reuptake inhibitor |
| **Stan** | starry night |
| **StAR** | steroidogenic acute regulatory protein |
| **STD** | sexually transmitted disease |
| **STI** | sexually transmitted infection |
| **stRNA** | small temporal RNA |
| **STS** | sequence tagged site |
| **SV** | seminal vesicle |
| **SVA** | seminal vesicle aspiration |
| **T1/2** | half-life |
| **TAC** | total antioxidant capacity |
| **TCA** | tricyclic antidepressant |
| **TDF** | testis-determining factor |
| **TDS** | testicular dysgenesis syndrome |
| **TdT** | terminal deoxynucleotidyl transferase |
| **TE** | testosterone enanthate |
| **TEFNA** | testicular fine needle aspiration |
| **TESA** | testicular sperm aspiration |
| **TESE** | testicular sperm extraction |
| **TET** | ten-eleven translocation |
| **TF** | tissue factor |
| **TGFβ** | transforming growth factor beta |
| **THC** | tetrahydrocannabinol |
| **TIMP-2** | tissue inhibitor of metalloproteinase-2 |
| **TJ** | tight junction |
| **TLR** | Toll-like receptor |
| **TM** | testicular microlithiasis |
| **Tmax** | time to maximum serum concentration |
| **TMSC** | total motile sperm count |
| **TNFα** | tumor necrosis factor alpha |
| **TRH** | thyrotropin-releasing hormone |
| **TRUS** | transrectal ultrasonography/ultrasound |
| **TSH** | thyroid-stimulating hormone |
| **TTP** | time to pregnancy |
| **TU** | testosterone undecanoate |
| **TUIED** | transurethral incision of ejaculatory ducts |
| **TUNEL** | terminal deoxynucleotidyl transferase deoxyuridine triphosphate nick end labeling |
| **TURED** | transurethral resection of the ejaculatory ducts |
| **UGCG** | UDP-glucose ceramide glucosyltransferase |
| **UGT** | UDP-glucuronosyltransferase |
| **ULC** | Uniform Law Commission |
| **UPA** | Uniform Parentage Act |
| **UPD** | uniparental disomy |
| **US** | ultrasound |
| **UTI** | urinary tract infection |
| **Vangl2** | Van Gogh-like 2 |
| **VDAC3** | voltage-dependent anion channel 3 |
| **VE** | vasoepididymostomy |
| **VEGF** | vascular endothelial growth factor |
| **VEGFr** | vascular endothelial growth factor inhibitor |

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| **VHL** | von Hippel–Lindau |
| **VR** | vasectomy reversal |
| **VV** | vasovasostomy |
| **VVSG** | Vasovasostomy Study Group |
| **VZV** | varicella-zoster virus |
| **WBC** | white blood cell |
| **WHO** | World Health Organization |
| **WPATH** | World Professional Association for Transgender Health |
| **YCMD** | Y chromosome microdeletion |
| **ZIKV** | Zika virus |
| **ZPBP** | zona pellucida binding protein |

# Introduction

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The last and fourth edition of *Infertility in the Male* was published in 2009, and significant advances were realized in reproductive medicine and surgery in the intervening decade. In this edition, we have covered the more recent advances in the field while maintaining the core foundation of information needed for practitioners in diagnosing and treating the man seeking care for fertility. We have also endeavored to make the book more structured, and hopefully easier to use, for the student and specialist alike.

For the first time, we have organized the book into sections: "Scientific Foundations of Male Infertility," the basic biological science undergirding reproductive medicine; "Clinical Evaluation of the Infertile Male," which covers clinical diagnosis; "Laboratory Diagnosis of Male Infertility," detailing laboratory diagnosis of testicular dysfunction and the basics of sperm cryopreservation; "Treatment of Male Infertility," describing the means and strategies for therapy for these diagnoses; and finally "Health Care System and Culture," which contextualizes male fertility care in society and the world. Many of these chapters have substantial overlap, as they consider topics from more than one perspective – while the chapter "Cryopreservation of Sperm – History and Current Practice" in the "Laboratory Diagnosis of Male Infertility" section attends to the history and laboratory processes of storing sperm for future use, "Male Oncofertility – Considerations for Fertility Preservation and Restoration" in the "Treatment of Male Infertility" section describes the conditions the clinician will encounter to utilize banking; "Sperm Retrieval Surgery" details how to surgically obtain sperm, and "The Use of Sperm in Medically Assisted Reproduction" explains how to use cryopreserved sperm in medically assisted reproduction techniques such as in vitro fertilization/intracytoplasmic sperm injection.

While chapters in the fourth edition included sentences in bold to draw the attention of the reader to their most pertinent parts, to facilitate the use of the book in practice, chapters now also include Key Points in boxes to facilitate and cement understanding and real-world use. Multiple related chapters in the fourth edition were combined – thus, although there are fewer chapters in this book, compared to its predecessor, they are deeper, more interrelated, and more understandable.

The section "Scientific Foundations of Male Infertility" begins, as did the previous edition, with a chapter detailing the anatomy and embryology of the male reproductive tract and gonadal development, the epididymis, and accessory sex organs, thus forming the basis of accurate anatomic diagnosis and surgery. The following chapter describes the complex interplay of cells and their communicating molecules that coordinate the production of sperm in the testis; its immediate succeeding chapter details how and what happens to sperm in the epididymis that makes them capable of fertilizing the ovum. As the male reproductive system is largely controlled by the endocrine system, a chapter follows describing the production and control of sex steroids in the male, laying the essentials for accurate endocrine therapy detailed later in the book. Once sperm is made, it must make its exit, and the chapter on erection, emission, and ejaculation then addresses these processes. Science never sleeps, and the final chapter in this section describes the enormous leaps in genomic modification and epigenetics during the last decade that are sure to be the foundation for diagnostic and therapeutic advances in the years to come.

The next section "Clinical Evaluation of the Infertile Male" brings our current knowledge of male reproductive pathology and its diagnosis to the armamentarium of the male fertility specialist. It begins with one of the most rapidly evolving areas in the field, our understanding of how other diseases are related to reproductive dysfunction, a chapter on "Infertility as a Metric of Men's Health." This presents one of the most important reasons why we care for male infertility – it may reveal significant underlying health conditions. Following is the chapter

"Office Evaluation of the Subfertile Male" that gives the practitioner concrete strategies to be used in the office encounter, including questions to ask, what to look for, and clinical interpretation of the semen analysis. As the field is unusual, in that two people are required for an outcome, "Evaluation of the Infertile Male's Partner" provides a high-level review of the diagnosis of the female. By reading it, the practitioner will have a clear understanding of the steps taken in parallel by the female fertility specialist in order to best integrate reproductive care. "Imaging the Male Reproductive System" provides the reader with when and how to use radiographic and ultrasonographic tools in the diagnosis of the infertile male and, importantly, when they are not necessary. Another area of explosive growth in the field in the past decade has been in our understanding of environmental toxicants and their effect on male reproduction, reviewed in "Effects of Environmental Chemicals on Male Reproduction." With "Endocrine Causes of Male Infertility – Diagnosis and Treatment," the foundation presented in the chapter detailing the male endocrine system in the prior section is carried forward into pathological endocrine states and how to diagnose them. The chapter "Spermatogenesis – Diagnosis of Normal and Abnormal States" provides an overview of spermatogenic pathology and its diagnosis, integrating the basic knowledge describing spermatogenesis in the prior section with related systems in this section, as well as providing context for treatment to be detailed more completely in a subsequent section on therapy. The chapter "Inheritance and Male Fertility" delineates genomic conditions manifesting as male reproductive dysfunction and carries forward the epigenetic background laid in the prior section into what practitioners need to consider in the clinic. Still bedeviling clinicians and patients alike, the commonly encountered varicocele is elucidated in the chapter bearing its name, including its history, pathophysiology, diagnosis, indications for treatment, and, as this chapter is targeted to a specific condition, the treatment itself. The section concludes with a chapter detailing infectious and immunological considerations in the diagnosis of male infertility, an often confounding area for those diagnosing and treating the infertile male. With a clear understanding of the material presented thus far, the practitioner is ready to diagnose any man presenting with infertility using the tools currently available in reproductive clinical science.

In the time-tested process of clinical evaluation of male reproductive dysfunction, the practitioner next obtains laboratory testing. The next section begins with an overview of the two pillars of reproductive laboratory assessment – endocrine and sperm – in "The Laboratory Evaluation of the Infertile Male" and provides a high-level overview of other topics such as sperm DNA fragmentation. These cutting-edge forms of assessment of male infertility are substantially expanded in the subsequent chapter "Advanced Diagnostic Approaches to Male Infertility" that details the myriad forms of sperm DNA integrity assays and which and when they are best used, and an encyclopedic list of currently known genomic defects affecting male fertility that are currently used for clinical diagnosis in some parts of the world. Sperm are dynamic cells, and the following chapter "Evaluating Defects in Sperm Function" describes the assays used in determining how well sperm swim and do their job in fertilizing an ovum. As the laboratory is critical in freezing sperm for future use, the final chapter in the section "Cryopreservation of Sperm – History and Current Practice" describes methods of preserving sperm, while contextualizing these techniques in their use both specifically as a therapy and broadly in a health care system.

With an understanding of the biological science of male reproduction and how to diagnose its dysfunction in the clinic and laboratory, the reader is now prepared to treat specific conditions of male infertility in the next section. The first chapter "Medical Treatment of Male Infertility" reviews endocrine therapy, nonendocrine medicines, and nutraceuticals. Should sperm be produced in the testis but encounter barriers to traversing and exiting the male reproductive tract, "Surgery to Improve Sperm Delivery" details the procedural methods to address the various causative problems. Should the making of sperm in the testis be at fault or it not be possible to alter the reproductive tract to deliver sperm, going to the source of sperm in the male gonad is necessary and the subsequent chapter "Sperm Retrieval Surgery" describes when and how to do so. If sperm is obtained from the testis or present in low quantities in the ejaculate, medically assisted reproduction is required and the chapter "The Use of Sperm in Medically Assisted Reproduction" details those methods, providing the practitioner with an understanding of what happens to sperm in the laboratory and beyond. During the past decade, a field coined "oncofertility" has expanded into a systematic approach to fertility preservation for cancer survivors, and the chapter bearing its name describes all aspects of this in great detail. The other side of fertility is when it no longer is desired, and the chapter "Male