

The Genetics of Ovotesticular Disorders of Sex Development

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INTRODUCTION

Disorders of sex development (DSD) encompass a very large spectrum of phenotypes, from minor malformations of the genitalia (hypospadias, cryptorchidism, hypertrophy of the clitoris) to sexual ambiguity. Taken together, these anomalies have an estimated frequency of 0.5–1% [1]. Moreover, DSDs have a major impact on quality of life. Recently, the debate about the management of patients with DSD has intensified over issues of gender assignment and the indication for early genital surgery. However, the scientific data on patient outcome have remained poor. The main obstacles to the optimal management of patients with DSD have been a combination of the lack of controlled outcome data and the lack of understanding of their pathophysiology, which prevents precise diagnostic categorization of patients. Despite much progress in the past 20 years, the molecular mechanisms underlying mammalian sex determination are still far from being understood, and the molecular basis of sex reversal in a large number of patients cannot yet be explained. DSDs can be divided into disorders of sex chromosomes, such as Klinefelter and Turner syndromes, disorders of hormone synthesis or action (such as androgen insensitivity syndrome in XY individuals or congenital adrenal hyperplasia in XX individuals), and disorders of gonadal development (such as XY gonadal dysgenesis or XX testicular or ovotesticular DSD [OT-DSD]). This chapter will focus on the latter (OT-DSD), formerly known as “true hermaphroditism”, which is defined by the presence of both ovarian and testicular tissue in the same individual. OT-DSD is one of the rarest forms of DSD, and one of the most poorly explained mechanistically. Within the disorders of gonadal development, that can also be called

disorders of sex determination, XY gonadal dysgenesis is typically caused by mutations in sex determination genes such as SRY, SOX9 or SF1; XX testicular DSDs are mainly (for 90% of them) caused by an X–Y translocation including the SRY gene. But the genetic etiology of OT-DSD remains unknown for a vast majority of patients.

PHENOTYPIC FEATURES OF OT-DSD

Gonads

The gonadal distribution of OT-DSD can be referred to as unilateral (ovotestis on one side and testis or ovary on the other), bilateral (ovotestis on each side), or lateral (testis on one side and ovary on the other) [2]. The most common form is unilateral, with ovotestis/ovary in 34%, followed by bilateral (ovotestis/ovotestis) in 29%, and lateral (ovary/testis) in 25%. The least frequent is unilateral with ovotestis/testis (12%) [3,4] (Table 7.1).

The position of the gonads in patients with OT-DSD corresponds to the amount of testicular tissue present, with a correlation between the degree of gonadal descent and the amount of testicular tissue. About half of the ovotestes are found in an abdominal position (with a quarter inguinal and a quarter labioscrotal), while almost all ovaries (85%) are abdominal and half of the testes are labioscrotal [3].

Geography

The geographical distribution of OT-DSD shows an overrepresentation in Africa, with the number of published cases at 17 per 100 million inhabitants, followed by Europe at 15.3, Asia is underrepresented at 1.2 cases per 100 million and South America at 3.6 per 100 million [3].

Genetic Steroid Disorders Chapter 7 The Genetics Of Ovotesticular Disorders Of Sex Development

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Genetic Steroid Disorders Hayk Barseghyan, Eric Vilain, 2013-08-22 Ovotesticular DSDs OT DSDs are disorders of sex development in which both testicular and ovarian tissues are present in the same individual We review the phenotypic variability of OT DSDs their sex chromosome constitution and their molecular genetics which remain for most patients poorly understood

Genetic Steroid Disorders Maria I. New, Bert O'Malley, Gary D. Hammer, Oksana Lekarev, Alan Parsa, Tony T. Yuen, Mone Zaidi, Ahmed Khattab, Anne MacDonald, 2023-06-14 Genetic Steroid Disorders Second Edition targets adult and pediatric endocrinologists clinical geneticists genetic counselors reproductive endocrinologists neonatologists urologists and psychoendocrinologists It is designed to assist these specialists in the diagnosis and treatment of steroid disorders This revision includes a new chapter on Gonadotropins Obesity and Bone and new research on non invasive prenatal diagnosis with cell free DNA Chapters are thoroughly updated covering steroid disorders the genetic bases for the disorder and case presentations This definitive reference belongs in every medical library Presents a comprehensive translational look at all aspects of genetic steroid disorders in one reference work Provides a common language for endocrinologists geneticists molecular pathologists and genetic counselors to discuss and diagnose genetic steroid disorders Saves clinicians and researchers time in quickly accessing the very latest details on genetic tests and diagnoses as opposed to searching through thousands of journal articles Highlights significant discoveries with clinical relevance presenting insight into which medications to use based on the genetic makeup of a patient Teaches the best strategies and most effective use of genetic information in the patient counseling setting

Endocrinology: Adult and Pediatric E-Book J. Larry Jameson, Leslie J. De Groot, 2015-02-25 Considered the definitive source in its field for over 35 years Endocrinology Adult and Pediatric has been thoroughly updated to reflect today's recent advances in adult and pediatric endocrinology Unique perspectives from a team of trusted world renowned experts ensure this medical reference book remains the most highly regarded text in the field Make the best clinical decisions with an enhanced emphasis on evidence based practice and expert opinions on treatment strategies Zero in on the most relevant and useful references with the aid of a more focused concise bibliography Locate information quickly while still getting the complete coverage you expect Now in full color with special design treatment for at a glance pediatric content helping to distinguish the pediatric content Expanded coverage for key topics such as pediatric endocrinology and obesity mechanisms and treatment in addition to today's hot topics in endocrinology including endocrine disruptors bariatric surgery androgen deficiency genetic causes of obesity endocrine rhythms and the use of tyrosine kinase inhibitors in thyroid cancer New content addressing the latest advances in testosterone and estrogen replacement as well as the new causes of calcium and phosphate disorders new molecular causes of endocrine cancers new genetic causes of reproductive disorders and more Updated clinical guidelines for diabetes lipid disorders obesity management osteoporosis and more as well as essential treatment updates for the medical management of acromegaly Cushing's Disease

hypercalcemia and diabetes mellitus New Key Points provide snapshots of what to expect in each chapter or serve as a refresher of what you just read Expert Consult eBook version included with purchase This enhanced eBook experience allows you to search all of the text figures references and videos from the book on a variety of devices Yen & Jaffe's Reproductive Endocrinology - E-Book Jerome F. Strauss, Robert L. Barbieri, Anuja Dokras, Carmen J Williams, S. Zev Williams, 2023-03-24 For over 40 years Yen Recurrent Pregnancy Loss Uterus Transplantation Mitochondrial Transplantation and Gene Editing and Germs Cells Developed In Vitro Provides extensively revised information on contemporary practices in assisted reproduction fertility preservation and ovulation induction Provides an online video library that highlights surgical procedures diagnostic imaging and functional ultrasound imaging Adds three new members to the exceptional editorial team Drs Anuja Dokras Carmen J Williams and Zev Williams Features full color high quality illustrations that clearly depict basic anatomic structures endocrine processes and cell function and dysfunction Includes bulleted lists under major headings in each chapter for quick at a glance summaries of every section Lists Top References at the end of each chapter that distill the most important references for research underpinnings to complement the complete online reference list An eBook version is included with purchase The eBook allows you to access all of the text figures and references with the ability to search customize your content make notes and highlights and have content read aloud Emery's Elements of Medical Genetics E-Book Peter D Turnpenny, Sian Ellard, Ruth Cleaver, 2020-12-15 Long recognized as a leading textbook in this fast moving field Emery's Elements of Medical Genetics and Genomics offers current complete information with a strong basis in practical clinical genetics and genomics for medical school and beyond The 16th Edition of this award winning text has been thoroughly updated throughout and includes case based and multiple choice questions end of chapter summaries an extensive glossary and convenient online access making it an ideal choice for all medical undergraduates as well as postgraduates seeking to improve their understanding and knowledge Includes new case based studies with questions and answers throughout in addition to multiple choice self assessment questions for study and review Covers key topics such as pharmacogenetics personalized medicine prenatal testing reproductive genetics and ethical and legal issues in medical genetics Divides the text into three easy to use sections The Scientific Basis of Human Genetics Genetics in Medicine and Genomic Medicine and Clinical Genetics Counseling and Ethics Features full color illustrations and other images that help readers visualize the appearance of genetic disorders and assist with the understanding of complex genetic structures Contains learning features such as summary boxes an extensive glossary of terms online hyperlinks to important genetics websites and clinical databases and more Presents the extensive knowledge and experience of distinguished editors Peter D Turnpenny and Sian Ellard as well as new editor Ruth Cleaver *Fanaroff and Martin's Neonatal-Perinatal Medicine E-Book* Richard J. Martin, Avroy A. Fanaroff, 2024-01-30 Selected for Doody's Core Titles 2024 in Pediatrics A must have reference for both general physicians and advanced practice providers Fanaroff and Martin's Neonatal Perinatal Medicine Diseases of the

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health needs of patients with congenital heart defects diabetes and cystic fibrosis Recognize diagnose and manage genetic conditions more effectively using an expanded section that covers these diseases disorders and syndromes extensively Find information on chronic and common dermatologic problems more easily with a more intuitive reorganization of the section

Nelson Textbook of Pediatrics E-Book Robert M. Kliegman, Bonita F. Stanton, Joseph St. Geme, Nina F. Schor, 2015-04-17 After more than 75 years Nelson Textbook of Pediatrics remains your indispensable source for definitive state of the art answers on every aspect of pediatric care Embracing the new advances in science as well as the time honored art of pediatric practice this classic reference provides the essential information that practitioners and other care providers involved in pediatric health care throughout the world need to understand to effectively address the enormous range of biologic psychologic and social problems that our children and youth may face Brand new chapters and comprehensive revisions throughout ensure that you have the most recent information on diagnosis and treatment of pediatric diseases based on the latest recommendations and methodologies Form a definitive diagnosis and create the best treatment plans possible using evidence based medicine and astute clinical experiences from leading international authors many new to this edition A NEW layout provides superior portability and exceptional ease of use Gain a more complete perspective Along with a broader emphasis on imaging and molecular diagnoses and updated references the new edition includes an increased focus on international issues to ensure relevance in pediatrics practice throughout the world Effectively apply the latest techniques and approaches with complete updates throughout 35 new chapters including Innovations in Addressing Child Health and Survival in Low Income Settings Developmental Domains and Theories of Cognition The Reggio Emilia Educational Approach Catatonia Refeeding Syndrome Altitude associated Illness Genetic Approaches to Rare and Undiagnosed Diseases Healthcare Associated Infections Intrapartum and Peripartum Infections Bath salts and other drugs of abuse Small Fiber Polyneuropathy Microbiome *Kingella kingae* Mitochondrial Neurogastrointestinal Encephalomyopathy Nonalcoholic Fatty Liver Disease Plagiocephaly CNS Vasculitis Anterior Cruciate Ligament Rupture and Sports Related Traumatic Brain Injury Recognize diagnose and manage genetic and acquired conditions more effectively A new Rehabilitation section with 10 new chapters including Evaluation of the Child for Rehabilitative Services Severe Traumatic Brain Injury Spinal Cord Injury and Autonomic Crisis Management Spasticity Birth Brachial Plexus Palsy Traumatic and Sports Related Injuries Meningocele Health and Wellness for Children with Disabilities Manage the transition to adult healthcare for children with chronic diseases through discussions of the overall health needs of patients with congenital heart defects diabetes and cystic fibrosis Understand the principles of therapy and which drugs and dosages to prescribe for every disease **Campbell Walsh Wein Urology, E-Book** Alan W. Partin, Roger R. Dmochowski, Louis R. Kavoussi, Craig A. Peters, Alan J. Wein, 2020-01-21 From the basic science underpinnings to the most recent developments in medical and surgical care Campbell Walsh Wein Urology offers a depth and breadth of coverage you won't find in any other urology reference Now in three manageable

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Harrison's Endocrinology, 3E Tinsley Randolph Harrison, 2013-04-29 Expansion of the endocrinology section of Harrison's principles of internal medicine

DeGroot's Endocrinology, E-Book R. Paul Robertson, 2022-09-29 Thoroughly updated to reflect today's recent advances in adult and pediatric endocrinology DeGroot's Endocrinology 8th Edition remains the comprehensive international reference of choice for today's endocrinologists and fellows A full peer review of the previous edition conducted by a largely new group of renowned editors was used to update this trusted two volume resource In depth coverage of both basic and clinical aspects of endocrinology and up to date information on the treatment and management of endocrine disorders are provided by a diverse group of expert contributors from six continents A full color format and helpful algorithms summarize clinical decision making and practical approaches to patient management Organizes content by all the glands that regulate the endocrine system while integrating basic science and clinical presentations of disease Includes new chapters Anatomy and Physiology of the Hypothalamus and Pituitary Differentiated Thyroid Cancer Medullary Thyroid Cancer Drugs that Affect Thyroid Function Genetic Disorders of the Adrenal Cortex Adrenal Pathology Primary Aldosteronism Transgender Healthcare Erectile Dysfunction Prevalence and Causes of Male Infertility Sexual Dysfunction in the Female Glucose Toxicity and Oxidative Stress Emphasizes basic science and evidence based practice throughout Features extensive updates to content on thyroid and adrenal dysfunction endocrine disrupting chemicals and human disease clinical management of diabetes and advances in genetics Includes algorithms to outline effective treatment protocols Contains new emphasis boxes that highlight key points in each chapter Enhanced eBook

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Twelfth Edition Review E-Book Alan W. Partin, Craig A. Peters, Louis R. Kavoussi, Roger R. Dmochowski, Alan J. Wein, 2020-01-09 With new and updated questions based on Campbell Walsh Wein Urology 12th Edition content this comprehensive review covers all the core material you need to know for board exam preparation and MOC exams From basic science underpinnings to the most recent developments in medical and surgical care more than 3 000 questions with detailed answers help you master the most important elements in urology The high yield bulleted format and identical chapter structure as the parent text are designed for efficient effective targeted review providing exactly the information you need for exam success Keeps you up to date with key topics covered in Campbell Walsh Wein Urology 12th Edition such as minimally invasive and robotic surgery advancements in urologic oncology including innovative therapeutics for personalized medicine new approaches to male infertility technological advances for the treatment of stones advances in imaging modalities and much more Covers new material on urinary tract imaging complications of urologic surgery urologic considerations in pregnancy urologic considerations in transgender individuals and more Provides more than 3 000 multiple choice questions and detailed answers including highlighted must know points in the answer explanations Includes additional study points at the end of each chapter as well as new pathology and imaging sections with review questions in relevant chapters Features interactive questions self assessment tools an extensive image bank and more on Expert Consult Helps you prepare for the written boards and MOC exams with confidence This reliable efficient review tool is written by the same team that has made Campbell Walsh Wein Urology the preeminent text in the field *Gynecologic and Urologic Pathology* Maria Rosaria Raspollini, Antonio Lopez-Beltran, 2019-02-21 This book highlights the similarities and differences in the pathology of the genital and urinary tracts in males and females **Williams Textbook of Endocrinology** Shlomo Melmed, MBChB, MACP, Kenneth S. Polonsky, MD, P. Reed Larsen, MD, FRCP, Henry M. Kronenberg, MD, 2015-11-30 For more than 65 years Williams Textbook of Endocrinology has been the gold standard in the field delivering authoritative guidance on every aspect of adult and pediatric endocrine system disorders The 13th Edition has been thoroughly updated by Drs Shlomo Melmed Kenneth S Polonsky P Reed Larsen and Henry M Kronenberg to bring you state of the art coverage of diabetes metabolic syndrome obesity thyroid disease testicular disorders and much more all designed to help you provide optimal care to every

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Genetic Steroid Disorders Chapter 7 The Genetics Of Ovotesticular Disorders Of Sex Development Book Review: Unveiling the Power of Words

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