



# Control of the onset of puberty

Sarantis Livadas and George P. Chrousos

## Purpose of review

The mechanism of puberty initiation remains an enigma, despite extensive research in the field. Pulsatile pituitary gonadotropin secretion under the guidance of hypothalamic gonadotropin-releasing hormone (GnRH) constitutes a *sine qua non* for pubertal onset. In turn, the secretion of GnRH in the human hypothalamus is regulated by kisspeptin and its receptor as well as by permissive or opposing signals mediated by neurokinin B and dynorphin acting on their respective receptors. These three supra-GnRH regulators compose the Kisspeptin, Neurokinin B and Dynorphin neurons (KNDy) system, a key player in pubertal onset and progression.

## Recent findings

The recent discovery that makorin ring finger protein 3 is also involved in puberty initiation provided further insights into the regulation of the KNDy pathway. In fact, the inhibitory ( $\gamma$ -amino butyric acid, neuropeptide Y, and RFamide-related peptide-3) and stimulatory signals (glutamate) acting upstream of KNDy called into question the role of makorin ring finger protein 3 as the gatekeeper of puberty. Meanwhile, the findings that 'neuroestradial' produced locally and endocrine disruptors from the environment may influence GnRH secretion is intriguing. Finally, epigenetic mechanisms have been implicated in pubertal onset through recently discovered mechanisms.

## Summary

The exact molecular machinery underlying puberty initiation in humans is under intensive investigation. In this review, we summarize research evidence in the field, while emphasizing the areas of uncertainty and underlining the impact of current information on the evolving theory regarding this fascinating phenomenon.

## Keywords

epigenetics,  $\gamma$ -amino butyric acid, gonadotropin-releasing hormone, inhibitory makorin ring finger protein 3, kisspeptin, KNDy system, neuropeptide Y, RFamide-related peptide-3

## INTRODUCTION

Puberty, the process of the maturation of a child into a sexually mature adult, is accompanied by a growth spurt and development of secondary sexual characteristics. It is clinically expressed by a cascade of morphologic, physiologic, and behavioral changes, all because of a gradual, progressive increase of gonadal activity. The mammalian reproductive system is vitally dependent upon pulsatile gonadotropin-releasing hormone (GnRH) release by a small population of GnRH neurons, which extend axons from the preoptic area and the infundibular nucleus (IFN) of the hypothalamus. These neurons act as the common output pathway integrating several internal and external cues, giving rise to pulsatile GnRH secretion, which subsequently regulates the pituitary–gonadal axis. The gradual rise of sex steroids signals puberty initiation and leads to development of secondary sexual characteristics [1\*].

The most striking feature of sexual development in primates is the long interval from birth until the initiation of the pubertal process, even though GnRH neurons are already mature at birth. Indeed, during the infantile period after birth, GnRH pulsatility is robust but subsequently decreases during childhood, recommencing at puberty [2]. It was initially believed that sex steroids sent an inhibitory signal to the hypothalamus during the juvenile period, an assumption based on experiments carried out in rodents, in which GnRH function is

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# The Control Of The Onset Of Puberty

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## **The Control Of The Onset Of Puberty:**

**Control of the Onset of Puberty** Melvin M. Grumbach, Gilman D. Grave, Florence E. Mayer, 1974 *Pediatric Endocrinology* Ora Hirsch Pescovitz, Erica A. Eugster, 2004 Pescovitz and Eugster both affiliated with the Section for Pediatric Endocrinology Diabetology at Indiana University School of Medicine provide essential information on the mechanisms diagnosis and management of pediatric endocrine disorders Aspects of human development and physiology are combined with information on etiology diagnosis and treatment Within each of the traditional endocrine systems contemporary molecular genetics and developmental endocrinology are presented followed by material on specific clinical disorders and therapeutic strategies Interspersed throughout the book are chapters devoted to emerging issues such as childhood obesity short stature and treatment of children with disorders of sexual differentiation B w photos and diagnostic images are included Annotation 2004 Book News Inc Portland OR booknews com source inconne *Williams Textbook of Endocrinology, 14 Edition: South Asia Edition, 2 Vol SET - E-Book* Shlomo Melmed, Ronald Koenig, Clifford J. Rosen, Richard J. Auchus, Allison B. Goldfine, 2020-06-30 *Williams Textbook of Endocrinology 14 Edition South Asia Edition 2 Vol SET E Book* *Williams Textbook of Endocrinology E-Book* Shlomo Melmed, Ronald Koenig, Clifford J. Rosen, Richard J. Auchus, Allison B. Goldfine, 2019-11-14 Expertly bridging the gap between basic science and clinical information *Williams Textbook of Endocrinology 14th Edition* brings together an outstanding collection of world renowned authors to provide authoritative discussions of the full spectrum of adult and pediatric endocrine system disorders New chapters and significant revisions throughout keep you up to date with recent advances in medications therapies clinical trials and more This essential reference is a must have resource for endocrinologists endocrine surgeons gynecologists internists pediatricians and other clinicians who need current comprehensive coverage of this multifaceted field Up to date with recent advances in medications therapies and clinical trials Provides state of the art coverage of diabetes metabolic syndrome metabolic bones disorders obesity thyroid disease testicular disorders newly defined adrenal disorders and much more all designed to help you provide optimal care to every patient Contains new chapters on Global Burden of Endocrine Disease Navigation of Endocrine Guidelines and Transgender Endocrinology Includes significant updates to the Diabetes section including a new chapter on Physiology of Insulin Secretion and greater coverage of Type 2 Diabetes Presents current information in a highly illustrated user friendly format for quick reference Enhanced eBook version included with purchase Your enhanced eBook allows you to access all of the text figures and references from the book on a variety of devices **Growing Up Forgotten** Joan Lipsitz, 1980-01-01 *Growing Up Forgotten* **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

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**Handbook of Psychology, Developmental Psychology** Irving B. Weiner, Donald K. Freedheim, 2003-01-03 This work provides an overview of cognitive intellectual personality and social development across the lifespan with attention to infancy early childhood middle childhood adolescence and early middle late adulthood Chapters cover a broad range of core topics including language acquisition identity formation and the role of family peers school and workplace influences on continuity and change over time **GnRH: The Master Molecule of Reproduction** Andrea C. Gore, 2002-04-30 Gonadotropin releasing hormone GnRH cells are the key regulators of reproductive function in all vertebrate organisms The GnRH molecule is synthesized in a small number of neurons in rostral hypothalamic regions of the brain In mammals these neurons release the GnRH decapeptide into the portal capillary system leading to the anterior pituitary gland There GnRH causes the release of the gonadotropins luteinizing hormone LH and follicle stimulating hormone FSH which in turn act upon the gonads to stimulate their maturation and to cause synthesis of sex steroid hormones estrogen progesterone and testosterone Although each of the levels of the hypothalamic pituitary gonadal axis is critical for reproductive function GnRH neurons play the primary role in the control of reproductive maturation and adult reproductive function and may even play a role in reproductive senescence Since its discovery in 1970 there has been intense interest in GnRH producing neurons with more

than 8000 papers and chapters in the last decade alone Despite this activity of research in basic and clinical science there has never been a book written specifically on GnRH neurons GnRH The Master Molecule of Reproduction aims to bring together the large and diverse literature of both laboratory and applied research that focuses on these unique cells This book will provide basic background into reproductive neuroendocrinology as well as specifics regarding the role of GnRH neurons in the control of reproduction Students studying endocrinology reproduction neuroendocrinology or molecular endocrinology will benefit from this book In addition this book will take a multi species approach which will be useful both to basic researchers as well as clinicians Whenever possible species differences and similarities will be presented and if possible studies on humans or the clinical relevance of basic research findings to humans will be discussed such as the treatment of reproductive disorders such as abnormalities in pubertal development or infertility

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**Knobil and Neill's Physiology of Reproduction** Ernst Knobil, Jimmy D. Neill, 2006 The 3rd edition the first new one in ten years includes coverage of molecular levels of detail arising from the last decade's explosion of information at this level of organismic organization There are 5 new Associate Editors and about 2/3 of the chapters have new authors Chapters prepared by return authors are extensively revised Several new chapters have been added on the topic of pregnancy reflecting the vigorous investigation of this topic during the last decade The information covered includes both human and experimental animals basic principles are sought and information at the organismic and molecular levels are presented The leading comprehensive work on the physiology of reproduction Edited and authored by the world's leading scientists in the field Is a synthesis of the molecular

cellular and organismic levels of organization Bibliographies of chapters are extensive and cover all the relevant literature

The Control of the Onset of Puberty. Edited by Melvin M. Grumbach, Gilman D. Grave [And] Florence E. Mayer ,1974

Control of the Onset of Puberty III Henriette A. Delemarre-Van de Waal,1989      Reproductive Technologies in Farm Animals, 2nd Edition Ian Gordon,2017-06-23 Building on the successful structure of the first edition the second edition of Reproductive Technologies in Farm Animals has been totally updated and revised to provide an up to date account of the key techniques employed in manipulating reproduction in farm animals including beef and dairy cattle pigs sheep goats buffaloes camelids horses and poultry A classic introductory text to the subject the book is based on a comprehensive review of the current literature This text remains key reading for students in animal science agriculture veterinary medicine and biology and veterinary practitioners and farmers who wish to keep updated on developments in techniques that may be useful in their daily practice      **Neuroendocrinology in Physiology and Medicine** P. Michael Conn,Marc E. Freeman,1999-10-06 A

panel of leading experts integrate the latest findings from basic and clinical science to create a comprehensive treatment of the processes by which the brain acts as an endocrine organ not only to control hormonal functions but also to maintain homeostasis and regulate behavior The authors recognized both as leaders in their fields and as skilled teachers provide systematic coverage of the analytical anatomical functional clinical and pathological aspects of neuroendocrinology Topics range from the interactions between the nervous and endocrine systems to the regulation of reproduction development metabolism fluid balance and biological rhythms Neuroendocrinology in Physiology and Medicine offers an unprecedented marriage of clinical and basic knowledge that has been missing from classical neuroscience endocrinology and physiology texts It will teach today s medical students and serve researchers as a valuable reference to this rapidly growing field

*Reproductive Biology of Teleost Fishes* Robert J. Wootton,Carl Smith,2014-10-17 Reproductive Biology of Teleost Fishes is the first integrated review of the reproductive biology of the bony fishes which are the most species rich and diversified group of vertebrates Teleosts display remarkable variation in their modes of reproduction and this volume is intended to provide a framework for understanding the remarkable reproductive diversity of this group It describes their reproductive biology using wherever possible phylogenetic analyses and life history theory as a means to interpret the information The book addresses the genetic physiological behavioural ecological evolutionary and applied aspects of teleost reproduction in a comparative framework that emphasises the adaptive basis of reproductive diversity Reproductive Biology of Teleost Fishes provides a comprehensive synthesis of fish reproduction that will be of great interest to life scientists particularly ecologists evolutionary biologists physiologists and advanced undergraduates postgraduates and research workers requiring a comprehensive overview of fish reproduction The book is suitable for courses in fish biology and ecology reproductive physiology and reproductive genetics It also addresses applied questions and will be of value for courses on fisheries science and aquaculture Libraries in all universities and research establishments where biological sciences fisheries science and

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## **Table of Contents The Control Of The Onset Of Puberty**

1. Understanding the eBook The Control Of The Onset Of Puberty
  - The Rise of Digital Reading The Control Of The Onset Of Puberty
  - Advantages of eBooks Over Traditional Books
2. Identifying The Control Of The Onset Of Puberty
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an The Control Of The Onset Of Puberty
  - User-Friendly Interface
4. Exploring eBook Recommendations from The Control Of The Onset Of Puberty



- Personalized Recommendations
- The Control Of The Onset Of Puberty User Reviews and Ratings
- The Control Of The Onset Of Puberty and Bestseller Lists
- 5. Accessing The Control Of The Onset Of Puberty Free and Paid eBooks
  - The Control Of The Onset Of Puberty Public Domain eBooks
  - The Control Of The Onset Of Puberty eBook Subscription Services
  - The Control Of The Onset Of Puberty Budget-Friendly Options
- 6. Navigating The Control Of The Onset Of Puberty eBook Formats
  - ePub, PDF, MOBI, and More
  - The Control Of The Onset Of Puberty Compatibility with Devices
  - The Control Of The Onset Of Puberty Enhanced eBook Features
- 7. Enhancing Your Reading Experience
  - Adjustable Fonts and Text Sizes of The Control Of The Onset Of Puberty
  - Highlighting and Note-Taking The Control Of The Onset Of Puberty
  - Interactive Elements The Control Of The Onset Of Puberty
- 8. Staying Engaged with The Control Of The Onset Of Puberty
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers The Control Of The Onset Of Puberty
- 9. Balancing eBooks and Physical Books The Control Of The Onset Of Puberty
  - Benefits of a Digital Library
  - Creating a Diverse Reading Collection The Control Of The Onset Of Puberty
- 10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
- 11. Cultivating a Reading Routine The Control Of The Onset Of Puberty
  - Setting Reading Goals The Control Of The Onset Of Puberty
  - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of The Control Of The Onset Of Puberty

- Fact-Checking eBook Content of The Control Of The Onset Of Puberty
- Distinguishing Credible Sources

### 13. Promoting Lifelong Learning

- Utilizing eBooks for Skill Development
- Exploring Educational eBooks

### 14. Embracing eBook Trends

- Integration of Multimedia Elements
- Interactive and Gamified eBooks

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