

Sarah K. Lyons
Marisa E. Hilliard
Editors



**Transitioning from
Pediatric to Adult Care
in Endocrinology**
A Clinical Handbook

 Springer

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Foreword

Life is often defined by recognizable stages which blend seamlessly as one progresses from birth to adulthood, senescence, and demise. Each person-defined stage, for example, infancy, childhood, adolescence, and young adulthood, has an element of time within accepted parameters, but not precisely the same in each individual, and is influenced by genetic endowment as well as the physical and cultural environment. The field of medicine has subdivided specialties of care by system or organ, in each case also by age; pediatric specialties serve populations distinct from adult caregivers in the same general discipline. Continuity of care was not an issue when major ailments limited or curtailed a normal life-span, as, for example, with diabetes before and during the early years of insulin therapy or adrenal insufficiency before the elucidation of steroid chemistry and the ability to treat with glucocorticoids and mineralocorticoids. But the spectacular developments over the past half century in diagnosing and treating endocrine-metabolic disorders and the ongoing and exciting developments in biotechnology, molecular biology, imaging, and video telecommunication promise even greater likelihood of extending high-quality life for those with congenital or acquired diseases of the endocrine (or other) systems. If so, how might one develop the optimum healthcare systems for continuity of care for those who have endocrine-metabolic disorders diagnosed and treated in childhood and who could look forward to more productive years as adults if only they receive appropriate care? Currently, there is a gap during the critical period of approximately 18–25 years, when for a variety of reasons, care provided by a pediatric service is not

always systematically transitioned to an adult service, with actual and potential serious consequences on immediate and future health.

This book is a “first of its kind” in addressing the question of how best to seamlessly transition adolescents who began treatment as children to appropriate adult care, recognizing the vulnerability and vagaries of young adult life as independence and maturity continue to grow. In their introduction, the editors describe the cultural and environmental challenges facing any adolescent, from which the adolescent with endocrine-metabolic disease is not immune, and the resulting additional burden on maintaining or achieving recommended medical targets. Those involved in the care of adolescents with type 1 diabetes have grappled with these problems for some time, and societies such as the American Diabetes Association and Endocrine Society have devoted considerable resources to developing guidelines which are described in two chapters. Less is known about transition to adult care in conditions such as congenital adrenal hyperplasia, Turner syndrome, evolving transgender issues, and long-term survivors of childhood cancers, an increasing constituency thanks to the improvements in treating childhood malignancies. The chapters on each condition are preceded by a section of general overview of the common challenges related to transition, as well as models of how transition might work operationally within the same or across separate healthcare systems. The greater experience of the editors and authors is with the populations and disorders as they pertain to the United States, including its health insurance structure which influences access, but where available and appropriate, the authors cite experience from other localities, principally from Europe (the United Kingdom, France, Holland, and Sweden). How healthcare transition should be addressed in non-European or less developed countries remains to be determined, and this book is likely to act as a stimulus for such efforts. As someone involved in the research, education, and care of endocrine disorders in childhood, I am pleased to see this field of scholarship becoming a prominent focus, recognizing

that such early steps inexorably lead to better care through the traditional scientific approach of hypothesis testing via carefully designed clinical trials. Moreover, such clinical studies are facilitated by the networking of centers with interest in and support for the issue of transition of medical care, in this case endocrine-related disorders. This book deserves a place as a resource on the library shelves in every endocrine center.

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Preface

The Transition Process

For health professionals caring for older adolescents and young adults with chronic endocrine conditions, providing consistent, effective, developmentally tailored care during the transition between pediatric and adult healthcare systems can be challenging. This clinical handbook provides pediatric and adult endocrinologists and multidisciplinary clinical professionals a practical guide to providing high-quality healthcare in the context of the complex transition process, understanding developmental and psychosocial issues of late adolescence and young adulthood, and pragmatic strategies to address these issues and support disease self-management.

While the terms “transition” and “transfer” are often used interchangeably in everyday conversation, they do not mean the same thing. Transition is more than the actual transfer of a patient’s care from pediatric to adult-centered health systems. Transition, as defined by Dr. Robert Wm. Blum in 1993, is “the purposeful, planned movement” of adolescents and emerging adults from child-oriented to adult-centered healthcare systems [1]. Transition encompasses pre-transfer preparation for transfer, the transfer event, and the post-transfer integration into the adult health system. Addressing transition in pediatric and adult subspecialty care is of the utmost importance, as serious medical and healthcare consequences can occur as a result of inadequate clinical attention during the transition process [2, 3]. Pre-transfer preparation efforts often occur during adolescence and incorporate patient and family education about how to take on increas-

ing responsibility for self-management of a complex chronic illness and how to access care within the adult healthcare system [4]. This book reviews published pre-transfer preparation and transition interventions and provides clinical strategies that can be integrated into routine care. Based on the available evidence about transition preparation and transfer to adult care, this book reviews clinical and care-related considerations for transition process from both the pediatric and adult perspectives and offers practical strategies to enhance the transition process and promote optimal outcomes, with applications across multiple endocrine conditions: type 1 and type 2 diabetes, Turner syndrome, congenital adrenal hyperplasia, endocrine sequelae of childhood cancer, and transgender care.

Ages and Stages During the Transition Period

This book focuses on the late adolescent and early adulthood years (roughly ages 16–30), with a recognition that adolescence starts several years prior and the ranges defining the upper limit of young adults can last until the late 30s [3, 5]. Of note, this book will primarily use the broadest terms to capture the transition period: “late adolescence and early adulthood” or “adolescents and young adults” (sometimes referred to by the acronym AYA). These terms are meant to encompass (but not be limited to) the developmental stage known as “emerging adulthood.” First conceptualized by developmental psychologist Dr. J.J. Arnett, emerging adulthood focuses on ages 18–25 and represents a distinct period in which young people are beginning to explore their options for adulthood and to adopt social and cultural responsibilities of adulthood, but have not yet achieved independence or met most milestones of later adulthood [6]. For the purposes of this book, we focus on the broader range, including the last years of adolescence and the first years of adulthood, as those years are when the transfer from pediatric to adult healthcare and establishment with an adult provider occur

most often [4] and when many shifts in residence, schooling, psychosocial issues, and health behaviors relevant to the process of healthcare transition (e.g., reproductive health concerns, risky behaviors) occur [6–9]. However, the transition process, including the preparation for the transfer to adult care, can begin much earlier; indeed, Got Transition/Center for Healthcare Transition Improvement recommends that the transition preparation process begins as early as 14 years of age [10], and this book will cover some disease-specific programs and approaches that begin in early adolescence.

Structure of This Book

This book is organized into two sections: the first five chapters present topics relevant to transition that have cross-cutting applicability across a number of endocrine conditions, and the last five chapters summarize condition-specific data and perspectives on transition-related care. In both sections, the purpose of the chapters is to provide an overview of the essential information for developmentally appropriate medical care during this challenging stage. To that end, the chapters focus on providing concise summaries of the literature, practical strategies for transition care for endocrine and other multidisciplinary providers, and links to useful resources and materials.

Chapter 1 presents an overview of the developmental period of late adolescence and early adulthood in relation to having and managing a chronic endocrine condition, including discussion of competing demands, common psychological symptoms and stressors that occur during this period, the roles of peers and family, and the development of self-management skills and health behaviors. Chapter 2 focuses on the relevant medical and healthcare issues that pediatric and adult endocrine providers should be aware of in their practice during the transition period, including risks for complications and comorbidities, the importance of screening and

treatment, healthcare utilization patterns (e.g., outpatient follow-ups and hospitalizations), gaps in care, privacy laws, insurance and healthcare coverage considerations, and medical issues that can arise with an inadequate transition process. Chapter 3 gives a review of transition-focused interventions and novel clinical approaches, including structured transition preparation programs, dedicated young adult clinics, transition navigators/coordinators, behavioral/supportive programs, and any other approaches to transition intervention across endocrine conditions. Chapters 4 and 5 focus on practical suggestions for pediatric and adult providers, respectively, caring for this population. Chapter 4 presents key issues pediatric providers need to be aware of related to transition, including professional organization guidelines for transition, preparation for transition as part of routine endocrine care, what patients/families want and receive in terms of transition, and practical recommendations. Chapter 5 presents key issues adult endocrine providers need to be aware of related to transition, including differences between pediatric and adult care, what patients want and receive from adult providers related to transition, considerations for receiving young adults into your practice, effective communication strategies, and practical recommendations.

Chapters 6, 7, 8, 9, and 10 are dedicated to special considerations, issues, and literature for six specific endocrine conditions: type 1 and type 2 diabetes, Turner syndrome, congenital adrenal hyperplasia, endocrine sequelae of childhood cancer, and transgender care. These conditions are highlighted as they are among the most common and challenging chronic endocrine conditions, are lifelong (usually diagnosed in childhood and persist into adulthood), and span pediatric and adult care. Patients with these conditions are at increased risk of poor health outcomes during the challenging transition years. The intent of these chapters is to provide a targeted overview of each condition and recommendations that may be integrated into care during the transition from pediatric to adult medical care. Each chapter highlights developmental and psychosocial issues relevant to the transition process for

young people with each condition, treatment and screening recommendations for medical care during this period, healthcare process issues such as locating care providers and navigating insurance issues, published transition care guidelines for each condition when available, and key resources to access for more information. We hope that this book provides a novel perspective on caring for people with endocrine conditions during the transition from pediatric to adult care.

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Contents

Part I Transition Issues Across Endocrine Conditions

- 1 Developmental Issues Associated with Emerging Adulthood 3**
Jodie M. Ambrosino
- 2 Medical and Healthcare Issues During Transition for Patients with Endocrine Conditions 25**
Surya Narayan Mulukutla and Kelly Fegan-Bohm
- 3 Transition Interventions and Clinical Strategies 51**
Jessica C. Kichler and Jessica Pierce
- 4 Pediatrics: Practical Considerations for the Transition Process 77**
Courtney N. Sandler and Katharine Garvey
- 5 Adult Care: Practical Considerations for Patients with Endocrine Conditions Transitioning from Pediatric to Adult Care 97**
Shivani Agarwal

Part II Transition Considerations for Specific Endocrine Conditions

- 6 Transition Considerations for Youth-Onset Diabetes (Type 1 and Type 2) 117**
Maureen Monaghan, Elizabeth A. Pyatak, and Jennifer Raymond

7	Transition Considerations for Turner Syndrome	139
	Sarah D. Corathers, Melissa Gerstle, Lori A. Casnellie, Colleen Pater, and Glynthia Trotman	
8	Transition Considerations for Congenital Adrenal Hyperplasia	161
	Bonnie McCann-Crosby	
9	Transition Considerations for Cancer Survivors with Endocrine Sequela	175
	Vincent Horne and Rona Sonabend	
10	Transition Considerations for Transgender Patients	195
	Diane Ehrensaft, Colton L. Keo-Meier, and Joanna Yuen	
	Index	221

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Part I
Transition Issues Across
Endocrine Conditions

Chapter 1

Developmental Issues Associated with Emerging Adulthood



Jodie M. Ambrosino

Many endocrine disorders originate in early childhood and therefore require years of follow-up with pediatric providers. Trust in these providers develops over time as successes accumulate and challenges are overcome. Naturally, the personal needs of these patients change as they grow and mature. Shifting this trust and care to adult providers is a critical task for emerging adults, who are charged with managing the demands of their disease along with the normative challenges of this transition to adulthood. For many, this is a difficult process and often leads to disruptions in healthcare and poor outcomes [1, 2]. It is in our best interest to understand more about this group of patients so that we can engage them in planning for their future with a chronic illness and help them reach adulthood in optimal health.

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Emerging Adulthood: A Unique Developmental Period

In 2000, psychologist Dr. J.J. Arnett introduced a paradigm shift with the developmental concept of “emerging adulthood” to capture and describe the impact that a postindustrial landscape and sweeping demographic changes in education, marriage, and childbearing have had on the transition to adulthood. Arnett demarcates and distinguishes the period from 18 to 29 years of age from the years of adolescence that precede them and young adulthood that follow them, highlighting this period as a distinct period of pronounced change, freedom, and individual exploration [3]. Key to Arnett’s theory is his claim that while emerging adults are legally independent in the eyes of the law and capable of self-direction, they are only semiautonomous and have not yet committed or settled into enduring adult roles in interpersonal relationships or work/careers. He adds that subjectively they describe themselves as being “in-between,” having exited adolescence, but not yet settled into a stable adult life where they are self-sufficient and completely on their own [3]. During this period, uncertainty and instability across many aspects of life are the new norm.

Psychologist Dr. JL Tanner takes Arnett’s description of emerging adults a step further and integrates the period of emerging adulthood into lifespan development. Moreover, she relies on the key concept of “recentering” to illustrate the internal shift that takes place as emerging adults become self-sufficient and better able to meet the demands of adulthood; daily behaviors directed largely by others (i.e., parent, teacher, and society) are increasingly self-regulated and self-directed. She outlines three stages during which emerging adults become progressively more oriented toward autonomy and independence while remaining connected to, but no longer embedded within, the family of origin. In so doing, emerging adults are expected to assume the responsibility for developing new social systems that can become the foundation for their adult development, adaptation, and growing success in adopting stable adult roles [4].

From the perspective of neuroscience, accompanying this shift are prominent brain changes that persist well into this period of emerging adulthood and create neural systems that strongly impact cognition and the development of important health behaviors [5]. During the mid-20s, prefrontal association cortices mature, and connections improve with neighboring limbic structures, making room for critical improvements in executive functions such as inhibitory control, focused attention, working memory, and cognitive flexibility [6]. Sensation-seeking and risk-taking behaviors carried over from adolescence gradually decline during the mid-20s, while calculated future-oriented behavior increases over the course of these years. Additionally, neural processing of incentives and rewards gradually shifts in sensitivity from positive to negative feedback, which drives a reduction in gratification and approach behavior and an increase in more effortful and delay/avoidance behavior [5]. For an emerging adult with a chronic endocrine illness, this means that they will likely be more selective in engaging in activities that could be detrimental to their health because they have the cognitive control and capacity to pause and weigh the short- and long-term benefits/consequences of their actions.

Taken together, the blend of risk-taking, novelty-seeking, and greater affiliation to peers that is common during late adolescence and early adulthood is specifically intended to help motivate an emerging adult to explore the world, despite its many unknowns and tremendous uncertainty. The integration of frontal and limbic systems and nearly mature executive functions that alter neural connections tempers these tendencies and can help prepare a person to grow more comfortable adopting adult roles. Moreover, the ability to mentally play with ideas, flexibly adapt to changing environments or unanticipated challenges, assert better self-control and resist temptations, as well as take the time to problem solve and consider what to do next enables emerging adults with demanding chronic endocrine conditions to exercise more thoughtful choices, set realistic goals, and better plan how to proceed in novel situations that optimizes their disease management [6, 7].

Competing Priorities Specific to Emerging Adults

During this time, emerging adults are faced with significant change and the task of balancing contrary forces on a larger scale than is experienced during adolescence. They experience the excitement of change, and its uncertainty; the freedom of being on their own, and the anxiety of managing responsibilities independently and competently; and the expansive opportunity to develop new relationships, and the potential for being isolated and alone. Emerging adults who live with chronic endocrine disorders must navigate these natural opportunities for growth with the logistic, lifestyle, and psychological challenges of also managing their chronic medical condition. Related educational, economic, career, and social priorities can compete with demands to manage a chronic illness and contribute to suboptimal healthcare utilization as well as delay the detection and/or treatment of medical and/or psychosocial challenges that can seriously impact quality of life [2, 8].

Significant milestones like graduating from high school, moving on to college, or starting a new job require the added responsibility of ensuring enough supplies and medications have been ordered to manage their illness for potentially protracted periods of time. Emerging adults also need to monitor their body for symptoms that might demand changes to their medication given their lifestyle change and adjustment to new surroundings. Consideration of transitioning the emerging adult from pediatric to adult care to facilitate access of appropriate follow-up care demands careful consideration of multiple factors since it is yet another significant change from what is familiar, foremost, the availability of a healthcare team with endocrine expertise. This can be a particularly confusing decision for emerging adults as they balance interest in wanting to be treated in a developmentally appropriate manner with the comfort and assurance that their team of providers understands their history and can comprehensively address their current needs [9].

Educationally and socially, shifts from high school to college and geographic relocations create a natural opportunity to “start over” and to be more selective about to whom and when to disclose their chronic medical condition. The motivation for this can be especially strong after having had little control as a child or adolescent over how others learned about one’s medical condition. Additionally, a history of bullying and/or peer conflict associated with one’s medical condition may have heightened the stigma of feeling different [10]. While this can create the opportunity for paced disclosure that maintains one’s privacy, controls the circumstances under which others are informed, and minimizes the chances for rejection, it may also introduce barriers to effective self-care. For example, college students who have not disclosed their condition to roommates, teachers, or the school may not get the support they need while away from home or be able to effectively self-advocate for accommodations that can support their academic success. Maintaining anonymity about one’s medical condition can also complicate the formation of social networks that can foster self-acceptance and act as a buffer from added stressors [11]. Consider the situation where a college student with type 1 diabetes disregards recommendations to limit alcohol consumption because they are out with new friends and don’t want to draw attention to their medical condition. They have a serious low blood sugar and require emergency assistance. This experience may heighten already existing concerns about being accepted, reinforce fear of hypoglycemia, and lead to isolation and depression. In contrast, aligning with college campus resources can facilitate connection with peers who may similarly cope with the daily demands of having a chronic medical condition [12, 13]. More frequent change in class/work schedules and routines on which disease-related management tasks are often anchored can also be very disruptive and lead to difficulty adhering to medication regimens until alternate arrangements (e.g., alarms) are made [13]. Lastly, health centers affiliated with academic institutions vary in their familiarity with chronic medical conditions. Emerging adults should be counseled to

assess the staff's level of experience at an institution's health center before they accept admission especially if they will be a distance from home.

Economically, emerging adults with chronic endocrine conditions may make employment decisions based more on practical needs to stay close to home or secure health insurance rather than on the promise or opportunity for professional growth that a job or extending their education might offer. This could negatively impact quality of life and impede the self-discovery so characteristic of this period of life. Some may not know that their chronic medical condition is a disability and/or be unaware of available legal protections, especially if they are not showing overt signs of their medical condition. However, according to the American with Disabilities Act (1990), any individual with a physical and/or mental impairment that substantially limits a major life activity is eligible for reasonable accommodations at school and in the workplace [14]. Laws at both the federal and state level offer protection against discrimination so that emerging adults with chronic endocrine conditions can have equal opportunities at school and/or are able to perform a job for which they are qualified. Even so, emerging adults may try to hide their condition and avoid engaging in self-care behaviors during their shift or workday. Depending on the type of work, this could increase their risk for injury and/or make them more susceptible to fluctuations in productivity associated with suboptimal disease management.

The ways in which emerging adults navigate these competing priorities can have lasting effects on their self-confidence and self-efficacy. Moving through college, completing internships, and/or starting new employment with appropriate accommodations can foster success, empower an emerging adult to advocate for themselves, and build important life skills critical to their adopting adult roles. In contrast, challenges along the way can be discouraging and build resentment. It is imperative that pediatric and adult health providers treating emerging adults with chronic endocrine conditions be attuned to these competing priorities and the difficulty

they may present for making disease management a high priority especially as they plan the transition from pediatric to adult care [15]. Setting unrealistic treatment goals that ignore individual circumstances can be invalidating and may undermine this fragile alliance, particularly if it is a new one. In contrast, being mindful of the differences in approach and delivery of healthcare between pediatric and adult patients and joining with the emerging adult to consider how their personal circumstances have influenced their decision-making can strengthen an emerging adult's capacity to problem solve and master the necessary skills to establish a healthy lifestyle [2, 15].

Lifestyle Behaviors During Emerging Adulthood

It is imperative for an emerging adult with a chronic endocrine condition to understand how to take care of themselves and demonstrate competency in self-management skills as they prepare to be on their own. While this includes their having a critical base of knowledge about the medical condition itself, it is equally important that they also appreciate the impact that more general lifestyle behaviors can have on their day-to-day functioning. Adhering to complex disease management regimens is difficult, especially when daily routines and schedules vary as they typically do for emerging adults. Engaging in other health-promoting behaviors, like exercising and/or meal planning, can feel like an added burden. For example, emerging adults with type 1 and type 2 diabetes need to learn how various types of exercise impact their blood sugars and for how long even after the activity is completed. This will enable them to experience the many health-promoting benefits that exercise offers, including a greater sense of well-being and improved physical fitness [16].

Knowing what to do for one's health is necessary; however, it is not sufficient for developing a healthy lifestyle. The gen-

eral literature consistently demonstrates that unfavorable patterns in lifestyle behaviors such as cigarette smoking, alcohol use, reduced activity level and sleep quality start during adolescence and peak in emerging adulthood [17]. Risk-taking, novelty-seeking, and reward-seeking behaviors remain characteristic of development for emerging adults because they have the freedom to explore the world, as well as the protection of not being fully immersed in adult roles. A recent review of 21 sources of nationally representative data found that compared to adolescents, young adults engaged at higher rates in a significant number of concerning health behaviors, including alcohol use, obesity, and cigarette smoking [17]. Nelson et al. also highlight evidence for weight-related behavior changes during emerging adulthood including reduced physical activity, increased fast-food consumption, and decreased fresh fruit and vegetable intake [18]. Adolescents and emerging adults with medical conditions similarly engage in risky health behaviors like alcohol and tobacco use [2]. For example, in a sample of 117 emerging adults with diabetes, 47.0% reported alcohol consumption, 29.9% reported binge drinking, and 34.7% reported smoking; rates were comparable for those without diabetes [19]. Carretier et al. also found that children and adolescent/young adult survivors of cancer have similar risk behaviors to their peers regarding tobacco and alcohol [20]. Engaging in unhealthy lifestyle habits like their peers may normalize life for emerging adults with chronic endocrine conditions; however, they also reduce health-related quality of life and increase morbidity and mortality [2, 21, 22].

Substantial evidence suggests that young adults are at an increased risk of problems if they are male, have substance-dependent parents, experience externalizing behaviors during adolescence, have favorable attitudes toward substance use, exhibit a lack of belief in conformity or the moral order, have low commitment to school, or were “early” users in adolescence [23]. According to a recent SAMHSA report, 18–25 years-old had the highest rate of alcohol dependence or abuse (16.3%) among people aged 12 or older [24].

Emerging adulthood is an important time for health promotion and disease prevention, especially for emerging adults in whom early, potentially reversible signs of complications from their chronic illness may surface [15]. As clinicians, we have the charge of keeping emerging adults engaged in healthcare so that we can detect these lifestyle and illness-specific risks that can impact adherence and health early on and offer appropriate medical and/or behavioral interventions that promote wellness and maximize lifelong functioning [25].

Coexisting Psychiatric Disorders Complicate Disease Management

Neuropsychiatric symptoms such as depression, anxiety, and cognitive dysfunction can be associated with some endocrine conditions like hyper- and hypothyroid disease so it is important to distinguish primary hormonal imbalances from psychiatric manifestations [26]. Similarly, transient mood fluctuations, mental status alterations, and changes in productivity and energy levels are biologically mediated symptoms that regularly accompany daily blood sugar changes among young adults with type 1 and type 2 diabetes. In fact, chronically elevated blood sugars often mirror symptoms of depression and can cause considerable distress (e.g., irritability, lethargy; changes in appetite, concentration difficulties). Collaboration between medical and mental healthcare professionals is important for treatment planning [27].

Beyond these circumstances where behavioral symptoms may be rooted in physiological changes, psychosocial challenges are quite common as emerging adults with endocrine disorders cope with unrelenting disease-specific, as well as more general, daily life stressors that can impact mood, raise uncertainty, and deplete personal coping resources. Emerging adults also face the added task of completing often burdensome self-care routines in new settings and planning for a future that can involve growing distance from family

and friends who know them well and on whom they have relied for daily support. Forming new trusting relationships with peers, co-workers, and even healthcare providers takes time, patience, and a willingness to be open to these new experiences.

Psychiatric disorders like anxiety and depression can complicate how effectively an emerging adult launches into adulthood and adapts to these psychosocial challenges. Anxiety can exaggerate uncertainty associated with existing threats (e.g., late disease effects/complications, recurrence) or new concerns, create doubt, and undermine confidence about being on one's own. Additionally, depression can color one's view of the future and drain a person of the hope that life is worth living.

Baseline rates of psychiatric illness for emerging adults are higher relative to other developmental periods. In the general population, lifetime prevalence estimates for 18–29 years-old indicate that anxiety (30.2%) and mood (21.4%) disorders account for over half of all psychiatric conditions [28]. More recent 12-month prevalence estimates for new cases of major depression episodes in emerging adults (18–25 years old) show that 12-month prevalence estimates have increased from 8.8% in 2005 to 9.6% in 2014, due largely to changes within the 18–20 year-old range [29]. Similarly, a cross-national study of college students (18–22 years old) showed that anxiety disorders were the most prevalent class of disorders across all groups (11.7–14.7%) followed by mood disorders (6.0–9.9%) and substance disorders (4.5–6.7%) [30].

For most emerging adults, these psychiatric problems do not develop during these periods of vulnerability but rather often carry over from childhood and adolescence. According to Auerbach et al., 83.1% of college students' disorders had pre-matriculation onsets [30]. Similarly, Kessler et al. found that half of all lifetime psychiatric cases started by age 14 years, and 75% by age 24 [28], while Copeland, Shanahan, Costello, and Angold found that by age 21, 61% of population-based study participants had met criteria for a psychiatric disorder [31].

Rates of comorbid psychological disorders like anxiety, depression, and eating disorders vary widely in emerging adults with chronic endocrine conditions. In terms of anxiety and depression, some studies report no differences from peers without medical conditions, while others report significantly higher rates [19, 32, 33]. Several methodological issues make it challenging to interpret these broad rates: (1) assessment strategies and periods of follow-up vary (e.g., different self-report symptom checklists, diagnostic semi-structured interviews); (2) data from emerging adults are often pooled with adults and difficult to isolate; and (3) considerable overlap exists between psychiatric symptoms and disease-related distress [2, 27, 34, 35].

Even though rates are controversial for anxiety and depression, it is important to be familiar with the possible ways in which emerging adults with specific chronic endocrine conditions can experience these symptoms and the impact that they could have on disease management. Anxiety can manifest as procedural distress, avoidance, non-adherence, disease micromanagement, hypervigilance to bodily symptoms, and worry about long-term health. For example, among people with type 1 diabetes, fear of hypoglycemia is associated with compensatory strategies of routinely running blood sugars high, which increases risk for poor glycemic control [36]. Among young women with Turner syndrome, differences in social competence can contribute to difficulty with interpersonal relationships and loneliness [37]. Similarly, frustration with unrelenting disease-related demands can cause burnout, characterized by feeling discouraged, overwhelmed, and reluctant to perform disease-related tasks. Burnout may be a precursor to depression. Prompt attention can help ameliorate these feelings, which could otherwise remain protracted, interfere with the transition to adult care, and contribute to poor long-term medical outcomes [27, 34, 38].

One of the most dangerous aspects of feeling distressed, trapped, and hopeless is suicide. After unintentional injury, suicide is the second leading cause of death for emerging

adults in the general population, ages 15–34. Moreover, 18–25 years-old had the highest rates of serious ideation (8.8%) and attempts (1.8%) [39]. Systematic reviews conducted with type 1 and type 2 diabetes patients indicated nearly doubled higher risks for suicide with both populations, although emerging adults were not separated [40, 41]. In the case of type 1 and type 2 patients, the irony is that they can use a lifesaving medication, insulin, to assist them in ending their life. In fact, the authors note that suicide-related deaths may be underestimated in diabetes patients and misrepresented as a severe hypoglycemic episode.

Similarly, there has also been a greater appreciation for and better recognition of the comorbidity of disordered eating and eating disorders in endocrine disorders, particularly type 1 and type 2 diabetes considering the complicated relationship between food intake, exercise, and the need for a lifesaving medication that can sometimes cause weight gain [42–44]. Coping with negative feelings about weight, shape, and body with restrictive or binge eating, purging, and/or insulin omission to optimize body image and assert control is a dangerous practice and poses a serious threat to health. A longitudinal study found that 32.4% of young adults with type 1 diabetes met the criteria for a current eating disorder, and an additional 8.5% (6/71) had a subthreshold ED; mean age at onset was 22.6 years [45]. The practice of insulin omission alone is associated with a threefold increase in mortality [46].

A gap between the need for and use of mental health services contributes to these sobering statistics and the high prevalence of psychiatric disorders. A substantial proportion of those identified as needing these services fail to receive any treatment at all [30, 47]. Furthermore, utilization declines precipitously at the age of emancipation [48], in part due to their aging out of child mental health systems and to their relocating for academic advancement and/or employment. Additional barriers relate to structural problems (e.g., lack of financial means/insurance copays, time constraints, various inconveniences) and attitudes (e.g., stigma, low perceived

efficacy of treatments, or the desire to handle the problem on their own) [47].

Treatment-related failures come at a high cost. For emerging adults, psychiatric disorders are strongly associated with subsequent college attrition [30], lower educational attainment [49], and significantly reduced earnings [29, 50]. Moreover, results suggest a dose-dependent effect whereby the higher the number of disorders, the greater the impairment, particularly for social life and close relationships [51].

Healthcare providers taking care of emerging adults with chronic endocrine disorders should be aware of the prevalence of these mental health disorders, as well as the synergistic effect they can often have on vulnerability to nonadherence and poor patient outcomes [52]. The apathy and hopelessness so characteristic of depression can contribute to a disregard for disease management and interfere with a timely transition from pediatric to adult care [38]. Screening programs can help identify these issues promptly so that appropriate referrals to mental health providers can be made swiftly when such comorbidities are suspected [16, 53]. This can also inform transition-related decisions for emerging adults preparing to exit pediatric care and ease the process of their assembling a new network of providers who can offer comprehensive care in this next phase of their disease management [54].

The Role of Family: Recentering, Changing Support Systems, and Self-Management

The time of diagnosis and complexity of treatment regimens for endocrine disorders vary widely depending on the condition and directly impact the degree of family involvement. Some endocrine disorders demand very active collaboration and oversight by parents and dynamic shifting in responsibility over time in keeping with a child's development, cognitive capacity, and readiness [55]. The practice of life skills such as

effective communication, problem solving, growing self-awareness, and conflict resolution is critical to a family's success in working well together [56]. Increasing opportunities to exercise independent use of these life skills provides invaluable learning and sets the stage for consolidation in the emerging adult, so that ultimately they have the capacity to manage themselves [15].

During emerging adulthood, support systems and interpersonal influences change significantly. Emerging adults need to construct new social systems outside their family of origin that can become the foundation for their adult development, that support healthy self-discovery, and that encourage the adoption of adult roles and personal intimacies [57]. In the context of these relationships, young adults practice their ability to regulate and adapt behavior to the demands of a situation and achieve personally chosen goals and values. Additionally, they appreciate the critical importance of accepting their medical condition, of integrating it into how they see themselves, and of recognizing that they do not have to be defined by their diagnosis.

This process does not often unfold smoothly, and layering comorbid mental health issues that also need to be managed complicates this process. It is essential to regularly evaluate and ensure that disease-related education provided during the adolescent years will adequately equip emerging adults to manage both their endocrine condition and mental health needs. In so doing, gaps that may exist, especially if they were diagnosed young, can be addressed, optimizing mastery of self-management skills and self-efficacy [58]. This should include careful planning ahead of time to determine how an emerging adult will either continue to see their existing pediatric providers or transition to accessible adult endocrine and mental health providers so there is no disruption in ongoing care and appropriate support is available in the event of a crisis [59].

It is important to consider that while the young adult is focused on strengthening the skills to be on his/her own, parents and/or caregivers may have their own reactions. Ending

longstanding relationships with family-centered health providers can be unsettling [60]. Caregivers could be acting from a place of fear in ways that undermine the burgeoning independence or from a place of hope that reinforces the natural processes underway. Healthcare providers can be sensitive to these conflicting feelings and assist parents in coping with them so that their emerging adult can venture into the world, despite the uncertainty, hopeful that new supports in place, as well as existing family alliances, will help them persevere [57]. Consideration always needs to be given to privacy laws so that releases of information can be discussed and mutually agreed upon ahead of time, honoring the role, albeit a changing one, that the parents/guardians still have in their emerging adult's life.

Conclusion

In summary, emerging adults who are maturing with chronic endocrine conditions face many challenges and competing priorities that can detract from management of their underlying endocrine condition. They are expected to play an increasingly more active role in their healthcare just as their medical and mental healthcare needs may be getting more complicated and confusing. This can be particularly stressful in the context of unstable routines and riskier lifestyles and contribute to ambivalence about adopting these adult roles. It is critical that pediatric and adult healthcare teams be familiar with and sensitive to these natural shifts occurring in autonomy and adoption of adult roles for an emerging adult, while also appreciating the mixed reactions that caregivers may be experiencing as they cope with their changing role. Pediatric and adult healthcare teams can act as leaders in designing developmentally appropriate and psychosocially sound care that is responsive to the needs of emerging adults, bridges pediatric and adult subcultures, and promotes ongoing engagement and the building of trust with proactive healthcare teams.

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Chapter 2

Medical and Healthcare Issues During Transition for Patients with Endocrine Conditions



Surya Narayan Mulukutla and Kelly Fegan-Bohm

Introduction

Transitioning from pediatric to adult healthcare systems can be a challenging process for all parties involved, including the adolescent/young adult patients, their parents or guardians, transferring pediatric physicians and medical teams, and accepting adult physicians and medical teams. Each party has their own assumptions and expectations regarding the most efficient and effective process to seamlessly transfer care. This chapter will emphasize the importance of continued engagement with the healthcare system and screening for complications, given the increased risk for acute and chronic complications that can arise from an inadequate transition process, resulting in worsening disease control in the face of

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25

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suboptimal healthcare utilization in the following endocrine conditions: type 1 and type 2 diabetes, Turner syndrome, congenital adrenal hyperplasia (CAH), endocrine sequelae of childhood cancer, and transgender care. It will also address issues specific to the transition period related to privacy laws, insurance and healthcare coverage, and medical issues that can arise when medical care is disrupted.

Screening and Treatment for Endocrine Disorders in Young Adults

Type 1 and Type 2 Diabetes

Adolescents and young adults with diabetes exiting pediatric care are uniquely vulnerable to worsening disease control. Recent data shows that within the pediatric age range, adolescents have the highest rates of poor glycemic outcomes [1]. Complicating matters, studies have shown that gaps in healthcare after transfer lead to decreased medical visits, which in turn are associated with worsening glycemic outcomes and higher rates of hospitalization [1]. Furthermore, the goal for HbA1c levels changes from $\leq 7.5\%$ for youth under age 18 to $\leq 7\%$ for adults [2, 3]. This tighter glycemic target starting in young adults aims to prevent diabetes complications.

Recommendations for when to start and how frequently to conduct screening for long-term microvascular complications of nephropathy, retinopathy, and neuropathy in type 1 diabetes and type 2 diabetes change between pediatric and adult healthcare (Table 2.1) [4–6]. Certainly, longer disease duration plays a critical role in increasing an individual's risk for complications, making adulthood increasingly risky over time [3]. This increased emphasis on annual screening in adult care can sometimes surprise young adults who are unfamiliar with the guidelines despite having had diabetes for a number of years.

In addition to insidious chronic complications associated with suboptimal glycemic outcomes, acute diabetes complica-

tions can also increase in incidence during the transition period [1, 7, 8]. Severe hyperglycemia or diabetic ketoacidosis (DKA) can be caused by a multitude of factors, including expectations for increased responsibility for self-management with less supervision than during adolescence, changes in alcohol or carbohydrate consumption, and changes in the amount or types of physical activity in which young adults engage [1]. Taken together, these factors may help to explain the increased incidence of DKA in adolescents and young adults (ages 18–25) compared to children and adults >25 years old [8]. Young adults have rates of DKA up to 2.5 times higher than elderly adults (>65 years) with a prevalence of 100–120 cases per 1000 in young adults compared to 38–60 cases per 1000 in elderly adults [8].

Hypoglycemia in type 1 diabetes is another serious acute complication, which can directly impact mortality. The Diabetes Control and Complications Trial (DCCT) reported that the adolescent group, aged 13–17 years at study entry and 20–24 years by study end, had higher rates of hypoglycemia (85.7 events/patient year) than participants who were adults at study entry (59.6 events/per patient year) [7]. The trend continues currently: among adolescents (<age 18) in the Type 1 Diabetes Exchange Clinic Registry in the United States, rates of severe hypoglycemic events were 7.1 per 100 patient years [9]. A relevant risk factor is alcohol intake, which is associated with worsening glycemic outcomes, and is often first introduced in the adolescent and young adult years [10].

Cardiovascular disease remains the major cause of morbidity and mortality for individuals with diabetes [11], making this screening extremely important during the transition to adulthood (Table 2.1) [4, 6]. Screening guidelines for blood pressure monitoring are similar between both pediatric and adult care providers with routine monitoring to be conducted at every visit. Though treatment thresholds are different between adults and children (reflecting pediatric criteria using height, age, and sex standards), the treatment of choice remains angiotensin-converting-enzyme inhibitors across the age spectrum [3, 11].

TABLE 2.1 Type 1 and type 2 diabetes screening recommendations in pediatric and adult care [4-6]

Condition	Pediatric care		Adult care	
	Screening target	Timing	Frequency	Timing
Type 1 diabetes	Nephropathy	After duration of 5 years	Annual	After duration of 5 years
	Neuropathy	After duration of 5 years	Annual	After duration of 5 years
	Retinopathy	Start at puberty or age ≥ 10 years, after duration of 3-5 years	Every 1-2 years	Within 5 years of diagnosis
	Lipids	First lipid panel "soon after diagnosis" (≥ 10 years of age)	Every 5 years, if normal	Starts at diagnosis
				At least every 5 years, if normal and < 40 years

Type 2 diabetes	Nephropathy	Starts at diagnosis	Annual	Starts at diagnosis	Annual
	Neuropathy	Starts at diagnosis	Annual	Starts at diagnosis	Annual
	Retinopathy	Starts at diagnosis	Every 1–2 years	Starts at diagnosis	Every 1–2 years
	Lipids	Starts at diagnosis (≥ 2 years of age)	Every 5 years, if normal	Starts at diagnosis	At least every 5 years, if normal and < 40 years

Given that type 1 diabetes is an autoimmune condition, there are varying recommendations from pediatrics through adulthood regarding screening for other autoimmune conditions such as thyroid disease, celiac disease, and less common adrenal insufficiency, hepatitis, dermatomyositis, myasthenia gravis, or vitamin B₁₂ deficiency. Recommendations for screening celiac disease occur soon after diagnosis, within 2 years after diagnosis, and again after 5 years, while recommendations for screening thyroid dysfunction are every 1–2 years even in asymptomatic children [4]. However, there are no other agreed upon periodic screening guidelines for asymptomatic individuals for less frequent autoimmune conditions as the effectiveness is unclear throughout the age spectrum [3, 12].

People with type 2 diabetes do not need screening for autoimmune conditions, but screening for conditions associated with obesity should be considered. Although no agreed upon screening guidelines are available, providers and patients should be aware of the need for continued assessment of polycystic ovary disease, hepatic steatosis, sleep apnea, and orthopedic complications given their strong association with obesity and impact on morbidity [3].

Finally, given that adolescence and young adulthood coincide with the first sexual experiences for many people, it is important for healthcare providers to address reproductive health during visits both in late adolescence and into adulthood. It can be easy to overlook this aspect of care: recent data show that <25% of women with diabetes aged 16–20 years old were aware of the maternal and fetal risks of pregnancy or the importance of HbA1c levels in preventing poor fetal outcomes [1].

Turner Syndrome

Turner syndrome affects approximately 1:2500 females and can impact multiple systems including endocrine, cardiovascular, and reproductive [13]. Up to 20% of women with

Turner syndrome are diagnosed in adolescence or later [14]. In addition to medical conditions associated with Turner syndrome, women with Turner syndrome are at increased risk of psychological distress including social isolation, anxiety, obsessive behavior, and low self-esteem [15, 16]. In addition, women with Turner syndrome can also have lower performance IQ due to issues with visual spatial skills, processing visual cues, social difficulties, and executive function [16]. Combined with the tremendous burden of a complex syndrome often requiring multiple specialists, these features of Turner syndrome become significant contributors to suboptimal health outcomes due to lack of follow-up and appropriate screening during the transition process [15]. Data from 150 women with Turner syndrome (mean age of 31 years) indicated that 45% lacked medical follow-up by any specialist for a mean of 12 years. Multiple comorbidities were thus “newly” diagnosed, including bicuspid aortic valve, aortic coarctation, aortic root dilatation, dyslipidemia, hypertension, and abnormal liver studies [17].

Given the multi-system involvement of Turner syndrome, screening recommendations in young women with Turner syndrome are summarized in Table 2.2 [15]. Adolescents and young adults with Turner syndrome should understand the importance of cardiovascular healthcare throughout the age spectrum. In addition to anatomical cardiac conditions, women with Turner syndrome are at increased risk of obesity, hyperlipidemia, diabetes, hypertension, stroke, and ischemic heart disease [14–16]. Hypertension is found in >30% of young girls and adolescents with Turner syndrome and more than half of adults with Turner syndrome [18]. Compared to age- and BMI-matched people, women with Turner syndrome have higher percent body fat coupled with larger waist circumference and lower percent lean body mass [15]. Rates of hyperlipidemia in Turner syndrome have been reported at 37–50%, significantly higher than the general population. The risk of developing type 1 diabetes is increased tenfold and type 2 diabetes fourfold [15]. Therefore, modifiable risk factors such as dietary education and appropriate physical activ-

TABLE 2.2 Turner syndrome screening recommendations in pediatric and adult care [15]

Screening target	Pediatric care			Adult care		
	Timing	Frequency	Timing	Timing	Frequency	Frequency
Thyroid function	Starts at diagnosis	Annual	Starts at diagnosis	Starts at diagnosis	Annual	Annual
Lipids	Per routine primary care guidelines	n/a	Starting at age 18 years with at least 1 risk factor	Starting at age 18 years with at least 1 risk factor	Annual	Annual
Liver dysfunction	After age 10 years	Annual	Starts at diagnosis	Starts at diagnosis	Annual	Annual
Diabetes (HbA1c)	After age 10 years	Annual	Starts at diagnosis	Starts at diagnosis	Annual	Annual
25OH Vit D	After age 9–11 years	Every 2–3 years	Starts at diagnosis	Starts at diagnosis	Every 3–5 years	Every 3–5 years
Celiac disease	After age 2 years	Every 2 years	“With suggestive symptoms”	“With suggestive symptoms”	As needed	As needed
Audiometric evaluation	After 9–12 months old	Every 3 years	Starts at diagnosis	Starts at diagnosis	Every 5 years	Every 5 years
Renal ultrasound	At diagnosis	n/a	At diagnosis	At diagnosis	n/a	n/a
Bone mineral density	After starting adult dose sex hormone replacement	Every 5 years	At diagnosis	At diagnosis	Every 5 years	Every 5 years
Transthoracic echocardiogram (TTE) or cardiac magnetic resonance scan (CMR)	Starts at diagnosis	Every 5 years	At diagnosis	At diagnosis	Every 10 years or prior to pregnancy	Every 10 years or prior to pregnancy
Exercise testing	n/a	n/a	Prior to pregnancy	Prior to pregnancy	n/a	n/a

n/a Not Applicable

ity should be emphasized as much as possible. In addition, across all ages, the relative risk of fracture is increased in Turner syndrome, and the risk of liver cirrhosis is increased fivefold [19].

Adolescents with Turner syndrome often develop primary ovarian failure. While 30% start puberty, only ~4% have menarche spontaneously [14, 16]. Treatment of primary ovarian failure requires estrogen and progesterone therapy. Women with Turner syndrome should understand the benefits of long-term estrogen therapy on vascular and bone health [15]: transdermal estrogen replacement may have a safer side effect profile, making this the preferred option [14–16]. Fertility consideration is extremely important while at a young age because among those with the ability to conceive spontaneously, it will decrease rapidly with age [15]. Therefore, the 2016 Turner syndrome clinical practice guidelines from the International Turner Syndrome Meeting in Cincinnati (henceforth, “the Cincinnati guidelines”) suggest offering fertility treatment/preservation at a young age [11]. The importance of multidisciplinary care including maternal-fetal medicine and cardiology is underscored in women with Turner syndrome contemplating pregnancy. The Cincinnati guidelines strongly encourage that all women with Turner syndrome be educated of the increased cardiovascular risk of pregnancy and those with high cardiovascular risk should be advised against pregnancy. Recommended tests prior to consideration of pregnancy are listed in Table 2.2 [15].

Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia (CAH) is most commonly due to 21-hydroxylase deficiency, and the overwhelming majority of children with CAH survive into adulthood. While classic CAH typically presents in the neonatal period, non-classical CAH often presents in adolescence or early adulthood due to less severe phenotypic gene variants [20, 21].

In a United Kingdom cohort of 203 adults with CAH (median age of 34 years), many individuals had short stature, obesity (41%), hyperlipidemia (46%), insulin resistance (29%), and osteopenia/osteoporosis (40%/7%) [21]. Moderate or severe hirsutism objectively graded by a health-care provider affected 27% of the women in this study. In addition, quality of life was significantly compromised due to “obesity or compromised sex life” [22]. People with 21-hydroxylase deficiency have a higher prevalence of adrenal tumors, including massive myelolipomas [23].

Therapy with glucocorticoids at all ages aims to avoid adrenal crisis but prevent over-virilization, although the goals of treatment in young adulthood are slightly different than childhood given the emphasis on growth in children. For adults, there is a balance between avoiding exogenous Cushing’s syndrome (weight gain, hypertension, pigmented striae, osteopenia) while maintaining fertility and suppressing menstrual disturbances in women and testicular adrenal rest tumors in men [20]. Glucocorticoid doses need to be monitored and decreased if clinically indicated given the changing goals of therapy across the age spectrum; however, many patients remain on their pediatric medication dosage and frequency, risking overtreatment [24]. No guidelines for screening for bone mineral density exist, though the risk likely stems from high doses of glucocorticoids. Consideration of dual-photon x-ray absorptiometry (DXA) in patients taking chronic dexamethasone 0.5 mg/d or higher, having Cushingoid stigmata, or following a long period of suppressed 17 hydroxyprogesterone and androgens is recommended [23].

Given that many patients with CAH have undergone gender assignment, gender reassignment, and/or genital reconstructive surgery, fertility considerations should be addressed early in treatment. Women who have undergone vaginal reconstruction are at risk for frequent bladder infections, vaginal stenosis, abscesses, cysts, or scar tissue [23]. Pregnancy success rates in female patients with classical and nonclassical CAH have been reported at 54% and 67%, respectively, and females with CAH have reported a high incidence of pain

during intercourse and lack of vaginal lubrication [22]. For women with CAH that become pregnant, >20% develop gestational diabetes [23].

In the United Kingdom cohort, erectile dysfunction was reported in 41%; 67% of males with CAH who sought fertility treatment were successful in conceiving. Of the small number of patients with testicular ultrasound imaging ($N = 16$), 11 (69%) had testicular adrenal rest tumors (TARTs) although less than one-half were palpable at clinical examination, making ultrasound an important diagnostic test in CAH-related male infertility [22]. Endocrine Society guidelines recommend periodic ultrasound screening for TARTs starting in adolescence [20]. TARTs are often reversible with glucocorticoid treatment as they are often the consequence of poor control of CAH, but some patients undergo gonadectomy [21].

Given the above issues with fertility as well as the inheritance pattern and prevalence of asymptomatic carriers (1:50–1:71), genetic counseling should be recommended at an early stage [20, 24]. Endocrine Society guidelines recommend genetic counseling for parents at birth of a child with CAH and for adolescents at the time of transition to adult care [20].

Endocrine Sequelae of Childhood Cancer

Thanks to multiple breakthroughs and overall improved quality of care, childhood cancer survivors are living longer. However, ongoing care is critical to manage medical sequelae that emerge in adulthood. The endocrine system is the most commonly affected syndrome in childhood cancer survivors: a 2013 study followed 310 adult survivors of childhood cancer for a median of 16 years and found that 48.5% of females and 62.8% of males were impacted by at least one endocrine disease [25]. Moreover, the risk of developing an endocrine condition increased with time from diagnosis [25, 26]: between age 18 and 30 years, the cumulative incidence of endocrine late effects tripled in males (24–72%) and almost doubled in females (26–50%) [25].

To detect, prevent, and manage the many risks for endocrine sequelae of childhood cancer and its treatment, the importance of screening and early treatment cannot be overstated. Specific risk-based screening guidelines, which take into account type/location of tumor as well as type/duration of therapy, should be used to ensure targeted hormonal testing at appropriate intervals (<http://www.survivorshipguidelines.org>) [27]. Since these sequelae can present years after completion of oncology therapy, often after transition from pediatrics to adult care, maintaining engagement in the healthcare system is necessary to routinely assess for signs and symptoms of endocrine dysfunction.

There are a number of possible endocrine sequelae of childhood cancer. Growth hormone deficiency is more likely among central nervous system cancer survivors, those that received cranial radiation or surgery, and those who received cancer treatment prior to attaining full adult height potential [25, 28]. Thyroid dysfunction includes hypothyroidism (primary or central), hyperthyroidism, and benign or malignant thyroid nodules. Thyroid surgery, radioactive iodine, and high doses of MIBG contribute to primary hypothyroidism. Apart from cranial surgery, risk of central hypothyroidism increases with escalating doses of cranial radiation (≥ 40 Gy) [28]. Similar to thyroid dysfunction, gonadal dysfunction can also arise from damage to the reproductive organs (testes or ovaries) or centrally. Of children with a history of bone marrow transplant (BMT), 53% of female survivors and 29% of male survivors have been reported to be hypogonadal, and it has been reported that 91% of the BMT survivors treated after age 13 developed hypogonadism [29]. Alkylating agents, heavy metals, and radiation to the testes, ovaries, pelvis, or total body have all been implicated in causing primary infertility in men and women [28]. Similar to pituitary dysfunction leading to thyroid disease, pituitary surgery and/or cranial radiation (≥ 30 Gy) increases risk for hypogonadotropic hypogonadism [28]. Adrenal function can be affected by cranial radiation with resulting central adrenal insufficiency. Annual screening is recommended for patients who received ≥ 30 Gy of cranial radia-

tion [28]. Radiation to the pituitary gland at very high doses as well as surgery near the pituitary/hypothalamus can also result in hyperprolactinemia and/or diabetes insipidus. Other late endocrine effects such as low bone mineral density and dyslipidemia are likely impacted by a multifactorial process related to chemotherapeutic agents such as corticosteroids and anti-metabolites, as well as other endocrine dysfunctions such as thyroid, gonadal, or growth hormone deficiencies [25].

Transgender Care

Transgender persons require multidisciplinary care, which include mental health, hormonal, and/or surgical therapy. It is important to note that not all transgender persons will desire treatment: some prefer partial or no treatment, while others advocate for complete gender transition. Transgender care is unique in that pediatric guidelines strongly recommend that certain aspects of the treatment plan including genital surgery involving gonadectomy and/or hysterectomy be delayed until young adulthood when the individual is of legal age [30]. In addition, treatment with sex steroids often takes many years to achieve the desired outcome, and consistent follow-up with routine monitoring is paramount. As such, treatment of transgender persons requires a successful transfer of care between providers.

Hormonal therapy involves pubertal suppression and/or cross-sex pubertal induction. For adolescents undergoing hormonal therapy, recommendations are to monitor height, weight, and blood pressure every 3–6 months and gender-specific laboratory data (Table 2.3) [30].

Sex hormone therapy carries risks which necessitate continued clinical monitoring and screening. For transgender females, risks include thromboembolic disease, macroprolactinoma, breast cancer, coronary artery disease, cerebrovascular disease, cholelithiasis, and hypertriglyceridemia. For transgender males, risks include erythrocytosis, sleep apnea, severe liver dysfunction, coronary artery disease, cerebrovascular disease, hypertension, and breast or uterine cancer [30]. In addition, both

TABLE 2.3 Transgender hormone therapy screening recommendations in pediatric and adult care [30]

Condition	Pediatric care		Adult care	
	Screening target	Timing	Frequency	Timing
Transgender males	Hemoglobin, hematocrit	Baseline and during induction of puberty	Every 6–12 months	Starting at baseline
	Lipids	Baseline and during induction of puberty	Every 6–12 months	Per routine guidelines for non-transgendered persons
	Testosterone	Baseline and during induction of puberty	Every 6–12 months	Until levels are in normal physiology male range
	25OH Vit D	Baseline and during induction of puberty	Every 6–12 months	Per routine guidelines for non-transgendered persons
	Bone mineral density	Baseline and during induction of puberty	Every 1–2 years	To continue until age 25–30 years or until peak bone mass reached
				Every 3 months during year 1 and every 6–12 months thereafter
				n/a
				Every 3 months
				n/a
				Every 1–2 years

Transgender females	Prolactin	Baseline and during induction of puberty	Every 6–12 months	Starting at baseline	“Periodically”
	Testosterone	n/a	n/a	Starting at baseline	Every 3 months
	Estradiol	Baseline and during induction of puberty	Every 6–12 months	Starting at baseline	Every 3 months
	25OH Vit D	Baseline and during induction of puberty	Every 1–2 years	Per routine guidelines for non-transgendered persons	n/a
	Bone mineral density	Baseline and during induction of puberty	Every 1–2 years	To continue until age 25–30 years or until peak bone mass reached	Every 1–2 years
<i>n/a</i> Not Applicable					

feminizing and masculinizing hormones in the presence of additional risk factors increase the risk of type 2 diabetes [31].

Given that the diagnosis of gender dysphoria uses *Diagnostic and Statistical Manual of Mental Disorders* (DSM) criteria for diagnosis and that transgender people are at high risk for significant psychosocial distress [32], the importance of mental health evaluations and referrals cannot be overstated. Transgender adolescents and young adults have more than a twofold increased risk of anxiety, depression, suicidal ideation, suicide attempts, and self-harm without lethal intent in comparison to cisgender people [32]. The diagnosis of gender dysphoria or gender incongruence should be revisited prior to initiation of masculinizing or feminizing treatment [33]. No assumptions by the healthcare team should be carried forward based on previous decisions. Feelings about fertility may also evolve over time and require new discussion, especially when decisions were made while the transgender adult was in pediatric care, but it is important to note that science in this area is still evolving.

Due to stigma, societal pressures, and other personal or financial reasons, transgender children and adolescents may not seek treatment, and adult providers may be initiating discussions of these issues. Though the prevalence of transgender adolescents is not known, studies in adults suggest that the prevalence could be as high as 1 in 200 people [32]. Finally, an important social factor which all providers should continue to explore is the family dynamic; transgender adolescents and young adults aged 16–24 years with “very supportive” parents have been shown to experience higher self-esteem, less depression, and fewer suicide attempts compared to people with parents who were “not supportive” [34].

Privacy Laws

Laws about personal healthcare information and who has the rights to access it have become increasingly complex with time. In 1996, congress passed the Health Insurance Portability and

Accountability Act (HIPAA), which mandates that personally identifiable health information be protected and kept secure and that individuals understand and control who accesses their health information [35]. However, HIPAA can be superseded by other state or federal laws if those laws are more restrictive. Although HIPAA mainly relates to patient information shared between healthcare settings, healthcare providers, and the organizations with which they conduct business (such as health insurance companies), there are also implications for daily practice in healthcare settings, especially in the context of transition of patients from pediatric to adult medical care.

For adolescents under the age of 18 years, information about their health and treatment plans are disclosed to parents/guardians with few exceptions since parents/guardians are the primary medical decision-makers. Typically, the only exceptions to these rules relate to contraceptive care, pregnancy-related care, or minors who are emancipated. However, each state has laws regarding what information healthcare providers are and are not required to share with parents/guardians of minors [36]. For example, in some states, a minor can access contraceptive services without a healthcare provider having to disclose this information to the minor's parent. In other states, only minors who meet specific criteria such as being married, a parent, or pregnant can access contraceptive services without a parent's consent [37]. To help healthcare professionals adhere to the current legal framework, the Guttmacher Institute (<https://www.guttmacher.org/united-states/teens>) provides comprehensive information by state on what health services minors are able to consent to without parental permission.

Beginning at age 18, young adults control their health information unless they are under a legal guardianship. A young adult's health information may not be released (e.g., lab results over the phone) to a parent, family members, and/or spouse without the young adult's written permission except in certain circumstances [38]. HIPAA outlines specifically what information must be included in a health information release such as

“the name of the person to whom the disclosure may be made,” “an expiration date or expiration event,” and “a description of the information to be used or disclosed” [38, 39]. However, in the context of a medical encounter, if a patient brings family members, friends, or spouses, a healthcare provider can share information with those present in the room if “the patient agrees or, when given the opportunity does not object” to a provider disclosing health information [40]. Therefore, it is important to give the patient an opportunity to excuse anyone present before health information is disclosed. If the patient agrees to the information being shared with whomever is present, written consent is not needed to disclose health information. More information on HIPAA can be found on the Health and Human Services website: <https://www.hhs.gov/hipaa/for-professionals/index.html>.

Being aware of the limits of privacy protections for young adults under the age of 26 who have health insurance through their parent’s plan is important for providers and young adults. Some contraceptive care and other medical care can be billed privately, but an Explanation of Benefits may disclose certain types of healthcare services or make the parent/guardian aware that healthcare services were accessed by the young adult. Some states have attempted to restrict information disclosed in an Explanation of Benefits to protect privacy, but not all of these laws have been successful [41]. Patients should be aware that this type of information disclosure is possible to ensure they understand that their parents may learn about their healthcare activities.

It is important for parents/guardians caring for young adults with intellectual disabilities (ID) or developmental delays (DD) that could impair their ability to make their own medical decisions to be aware of their state’s laws regarding the age of majority and when they will be considered able to consent for themselves and their own healthcare decisions. According to HIPAA’s regulations, patients have control over their information unless consent is granted to give family members access or, as in the case of a legal guardian, control (a legal designation where the guardian is allowed to make all

decisions without input from the young adult who does not have capacity for decision-making) [35]. The Arc (a national non-profit group advocating for those with ID/DD) recommends that “less restrictive means of decision-making supports (e.g., healthcare proxies, advance directives, supported decision-making, powers of attorney, notarized statements, representation agreements, etc.) should be tried and found to be ineffective in ensuring the individual’s decision-making capacity before use of guardianship as an option is considered” [42]. This stance helps to ensure that young adults who are able to collaboratively make decisions with family members/health representatives do so without the limitations set forth by legal guardianship.

Privacy laws are intricate and do not always take into account the complexities of how patients and their families work together to manage complex chronic diseases. It is important for healthcare providers to have working knowledge of the context in which information can be disclosed once an adolescent reaches the age of majority. Giving adolescent patients and their parents information on the changes in privacy practices that will occur at age 18 is essential for patients, their families, and their physicians to have a successful working relationship.

Health Insurance

Uninterrupted healthcare for adolescents and young adults with chronic medical conditions is essential, but young adults are vulnerable to gaps in healthcare coverage. Since the enactment of the Affordable Care Act (ACA) in 2010, insurance coverage rates have improved across groups, but gaps still remain, especially for young adults. In 2016, the percentage of 19–25 years-old without health insurance was 13.1% [43]. In individuals with chronic diseases, gaps in medical coverage could lead to a lack of access to appropriate healthcare services including medications, health screenings, and appropriate follow-up with healthcare providers.

Many healthcare providers do not receive training on the different forms of medical coverage available in the United States and may not feel adequately informed to accurately advise their patients on how to prevent gaps in their care. It is important to be aware of major time points where young adults are at risk for gaps in care. Figure 2.1 lists some major milestones for healthcare coverage during adolescence and young adulthood that providers should be aware of in order to help them prepare and plan for ways to maintain coverage (Fig. 2.1).

In general, most publicly funded programs for medical coverage such as Medicaid or CHIP provide coverage through age 18 [44]. Some states extend coverage under these programs for young adults with disabilities, those who have been in the foster care system, or other special circumstances, but these vary by state; it is important for young adults to find out what they may be eligible for based on the state where they reside. For young adults who are covered by their parent's military insurance, coverage typically extends through age 21 unless the young adult meets specific eligibility criteria [45]. Through ACA, parents with private insurance can add their children until age 26 onto their plan. If a young adult

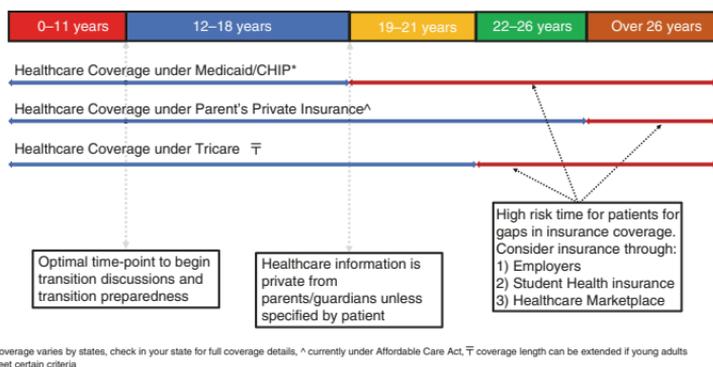


FIGURE 2.1 Timeline of important healthcare events in adolescents and young adults. *Coverage varies by states, check in your state for full coverage details, ^currently under Affordable Care Act, coverage length can be extended if young adults meet certain criteria

does not have a coverage option through public insurance programs or parental insurance plans, other options include buying private insurance through the healthcare exchange, enrolling in health insurance through their school (if they are currently attending college), or obtaining coverage if available in their workplace. Patient resources for healthcare coverage include:

- <https://www.healthcare.gov/young-adults/> – Frequently asked questions about healthcare coverage for young adults
- <http://illinoisap.org/wp-content/uploads/DoYouUnderstandInsurance.pdf> – Fact sheet from the Illinois Chapter of the American Academy of Pediatrics with some basic information about health insurance coverage

Summary

As adolescents and young adults with chronic illnesses transition from pediatric to adult care, it is important that they receive age and developmentally appropriate medical care and remain engaged in the healthcare system. Close follow-up is necessary during transition, and screening for comorbidities is dependent on the condition. Educating patients regarding changes in privacy laws and healthcare coverage is imperative.

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Chapter 3

Transition Interventions and Clinical Strategies



Jessica C. Kichler and Jessica Pierce

Healthcare transition from child to adult care encompasses a significant shift in medical care approaches. Differences between child and adult care can be summarized into four broad categories: focus of care (short-term versus long-term complication prevention), patient-provider relationship strategy (interaction with the whole family versus interaction with the adult alone), treatment approach (multidisciplinary providers always available versus individualized treatment with some multidisciplinary providers available upon request/need), and identified patient population (children and adolescents versus older adults with multi-morbidities) [1].

In addition to a fundamental shift in medical care approaches for children versus adults, there are three general healthcare transition models outlined in the literature which describe how to transfer adolescents and young adults' medi-

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cal home from child to adult care [2]. The first model is transitioning adolescents and young adults from pediatric care to adult providers within the same health system, but there is a change in providers (i.e., same health system, new providers). A second model is to transition adolescents and young adults to adult-focused care without changing providers, so the patient stays in the same care system, but the provider changes their clinical approach (i.e., same health system, same providers). A third model is the integration of adolescents and young adults into adult care in a new health system with new providers (i.e., new health system, new providers). Finally, an emerging fourth model, used most frequently in specialty care settings, is a joint pediatric-adult care model in which the patient is seen by existing pediatric care providers together with new adult care providers. This approach can occur in the same, pediatric setting or in a new, adult-based setting (i.e., same or new health system, same and new providers; see Table 3.1) [3].

Regardless of the healthcare transition model used, there are well-established recommendations for components to include in these healthcare transition programs. The National

TABLE 3.1 Transition to adult care models [3]

Type of practice	Care location	Providers
Practices serving youth who will transition out of pediatric care and into adult care	Same health system	New providers
Practices serving youth who will remain with the same provider but need to transition to adult-focused medical care	Same health system	Same providers
Practices accepting new young adults into adult care	New health system	New providers
Joint pediatric-adult care for youth as an intermediate step between pediatric and adult care	Same or new health system	Same and new providers

Committee for Quality Assurance (NCQA) in the United States proposes six core elements for transition, (1) Young Adult Transition and Care Policy, (2) Young Adult Tracking and Monitoring, (3) Transition Readiness/Orientation to Adult Practice, (4) Transition Planning/Integration into Adult Practice, (5) Transfer of Care/Initial Visit, and (6) Transfer Completion/Ongoing Care, and provides online “Got Transition” tools (<http://www.gottransition.org/>) for implementing each core element [2]. There is a similar model in the United Kingdom (“Ready Steady Go”) at the National Health Services teaching hospital, which uses an “empowerment” approach through the completion of a series of questionnaires by adolescent and young adults [3].

Researchers identified common factors that contribute to successful healthcare transitions in adolescents and young adults to build a theoretical framework for understanding transition readiness across various chronic conditions, including both individual and contextual factors (e.g., acquired skills, beliefs, and knowledge about their chronic condition) within the context of the healthcare system [4]. However, most of the existing clinical research on healthcare transition uses measures that assess the adolescent and young adult’s ability to complete general health management tasks (e.g., refilling a prescription). These general measures are not always relevant to the health outcomes associated with particular chronic medical conditions and do not always represent the specific components of a healthcare transition intervention program that has been developed to facilitate the transfer from child to adult care within a specific condition. Additionally, measures of healthcare transition outcomes vary among studies (both within and among chronic conditions), making it difficult to generalize and compare findings [5].

Similar to other chronic medical conditions, seamless healthcare transitions for adolescents and young adults with endocrine conditions are suboptimal across the world [6], with lost to follow-up rates ranging from 21.7% to 36.8% after leaving pediatric care [1]. During healthcare transition

for adolescent and young adults with endocrine disorders, medical complications can occur if hormonal treatment is not adequately maintained, including reduced or loss of physical and cognitive functioning and even death, as well as the loss of anticipatory guidance/screening for other disease-specific considerations (e.g., comorbid cardiac issues and preservation of fertility interventions) which can impact the trajectory of the adolescent and young adult's adult life [1]. Barriers to successful healthcare transition can be characterized as (1) differences between child and adult medical care approaches (see above), (2) difficulty with the transfer of responsibility for medical care from the parent/caregiver to the adolescent and young adult, and (3) logistical issues around healthcare navigation within the new health system [1, 6].

In the following sections, transition interventions and novel clinical approaches for six populations of patients, who receive regular endocrine treatment during the healthcare transition time period, are discussed (i.e., type 1 and type 2 diabetes, Turner syndrome, congenital adrenal hyperplasia, childhood cancer, and transgender care). Specifically, a wide variety of healthcare transition models, including structured transition preparation programs, dedicated young adult clinics, transition navigators/coordinators, and behavioral/supportive programs that contribute to the growing clinical implementation literature for a successful healthcare transition, will be highlighted.

Type 1 Diabetes

For adolescents and young adults with type 1 diabetes, a wide variety of pre-transition factors (e.g., not meeting glycemic goals, less education, and younger age) are related to negative post-transfer outcomes, yet healthcare transition preparation interventions do not always ameliorate these outcomes [7]. The American Diabetes Association (ADA) published transition guidelines in 2011 [8], yet a more rigorous evaluation of current healthcare transition programs is needed to deter-

mine which of the key components may contribute to a successful post-transition outcomes for adolescent and young adults with type 1 diabetes [5, 9]. Specifically, early preparedness, more developmentally appropriate structured transition programs, and improved professional connections between pediatric and adult care providers have been recommended in the literature, but not fully examined empirically [10].

Most of the literature on healthcare transition in diabetes focuses on adolescents and young adults with type 1 diabetes who are seen in pediatric diabetes programs that are housed in children's hospital settings. The overarching healthcare transition model for this population is the integration of adolescents and young adults into a new health system, with a new provider (see Table 3.1). A variety of structured transition program options for this type of healthcare transition model are summarized in the literature [9, 11, 12]. Four main approaches to implementing this type of healthcare transition model have emerged, including (1) transition preparation within pediatric diabetes clinics, (2) separate adolescent and young adult clinics which are jointly run by pediatric and adult care teams, (3) adult care-based transition programs for those receiving the pediatric patient transfers, and (4) distinct interventions provided outside of routine diabetes clinics.

Transition Preparation in Pediatric Clinics

Pediatric transition readiness programs for adolescents and young adults with type 1 diabetes are multifaceted and often include a formal transition curriculum with transition readiness educational materials and assessments, as well as targeted interventions from the diabetes care team. For example, healthcare professionals at Rush University Medical Center [13] developed a quality improvement initiative based on the "Got Transition" model and ADA transition recommendations and evaluated transition readiness using the Transition Readiness Assessment Questionnaire (TRAQ) [14]. By extracting data from a transition registry, the authors found

that the patients' TRAQ scores were not correlated with glycemic levels and that participants had lower confidence in maintaining appointments and tracking health issues but that participants did report confidence in completing daily self-management tasks [13]. At the Children's Hospital of Wisconsin/Medical College of Wisconsin, providers in the pediatric diabetes clinic developed a "Moving On" transition program in which a majority of the education is integrated within regularly scheduled pediatric diabetes clinic visits along with supplemental options for families to attend formal transition education classes, coordinating with early or late adolescence [15]. In a subsample of parent-adolescent/young adult dyads, participants reported self-efficacy for adolescents was not related to glycemic levels, and only about half of the participants used the supplemental resources offered in the "Moving On" transition program. However, both parents and adolescents/young adults indicated high self-efficacy and diabetes knowledge [15]. Using the "Let's Empower and Prepare" (LEAP) Program, the pediatric diabetes clinic at the University of Southern California enrolled adolescents and young adults in their last year of pediatric care into a transition readiness program that provided support from a case manager trained in healthcare transition-related issues. These adolescents and young adults were also given the option to participate in an adolescent and young adult-specific diabetes clinic, attend additional diabetes educational classes, and have access to a social networking website prior to transfer to adult care [16]. This LEAP Program was also found to be a promising intervention (e.g., improved glycemic levels, decreased hypoglycemia events and emergency room visits, and increased number of clinic visits) for a subset of these adolescents and young adults who had lapses in care during the healthcare transition [17].

Separate Adolescent and Young Adult Clinics

Specialized adolescent and young adult diabetes clinics provide developmentally appropriate care as an intermediary step between pediatric and adult care and are usually jointly run by

both pediatric and adult care teams (i.e., joint pediatric-adult care model; see Table 3.1). For example, at Winthrop Comprehensive Diabetes Care Center where pediatric and adult patients with diabetes are served in two distinct clinics within the same health system, adolescent and young adult patients are seen in a single, structured joint diabetes clinic visit, prior to transferring to a new adult provider [18]. This structured transition process yielded improvements in attendance to follow-up clinic visits and reductions in diabetes-related distress from pre- to post-transition [18]. Similarly, at the Sheba Medical Center in Israel, where both pediatric and adult diabetes care are provided in the same health system, a separate adolescent and young adult clinic was created with the support of a transition coordinator (i.e., an administrative person to aid in the logistics of navigating the health system). These joint clinics included a pediatric endocrinologist, nurse, and psychologist as well as an adult endocrinologist and registered dietitian and yielded improvements in glycemic levels and increased visit attendance (i.e., three or more visits per year) [19].

Adult Care-Based Transition Programs

Since adult providers are the ones receiving and taking responsibility for the adolescents and young adults' medical care upon transfer (i.e., new health system, new provider model; see Table 3.1), effective adult care-based transition programs are much needed. One such model is the Pediatric to Adult Diabetes Transition Clinic at the University of Pennsylvania which includes six program components (care coordination from pediatric to adult care, orientation to adult healthcare expectations, continuing education for diabetes self-care, behavioral support around barriers to self-management, engagement in care through shared decision making, and a partnership with pediatric providers by providing feedback on transferred patients for future program development) [20]. This program yielded promising results for transition outcomes (e.g., increased blood glucose checking frequency, improved diabetes clinic visit attendance to at

least two visits in a 6-month time period, and high ratings of program satisfaction) for adolescents and young adults with type 1 diabetes [20].

Transition Interventions Distinct from the Diabetes Clinic

Regardless of whether the healthcare transition occurs within the pediatric setting, as a part of a separate adolescent and young adult clinic setting, or in an adult care setting, some additional innovative healthcare transition interventions exist. These interventions can occur outside of the routine diabetes clinic visits and may include transition coordinators (health system navigators/case managers), individual and group-based diabetes education classes, and/or Internet-based disease management interventions. These interventions may augment other structured transition programs [15–17, 19] or be stand-alone interventions. In Australia, the Sydney Children's Hospital at Westmead implemented transition coordinator support via telephone for 12 months prior to the healthcare transition to adult care with promising outcomes, including retention in adult care following transfer [21]. Other interventions outside of the diabetes clinic setting also include professionally led young adult support groups and may provide utility for improving diabetes outcomes (e.g., improvement in achievement of glycemic goals, decrease in reported diabetes burden) in adolescents and young adults during this high-risk time [22]. The development of technology-based transition intervention programs for adolescent and young adults' chronic disease management has shown that less resource-intensive and non-disease-specific interventions may also be valuable tools in improving self-management, self-efficacy, and patient-initiated communication with healthcare providers for adolescents and young adults with type 1 diabetes [23].

Much of the research in healthcare transition approaches for adolescents and young adults with type 1 diabetes supports the national ADA recommendations that transition program-

ming should be gradual, integrated, and longitudinal in order to help adolescents and young adults with diabetes transition from pediatric to adult care. It is the responsibility of all diabetes providers – pediatric, adolescent, and adult specialists – to develop transition programs not only to meet the national standards of care, but to also focus on being patient-centered, incorporate general transition materials (e.g., from the “Got Transition” program), promote provider communication across pediatric and adult diabetes clinics, and improve the ease of healthcare navigation to minimize the number of adolescents and young adults with diabetes lost to adult care follow-up.

Type 2 Diabetes

There is a paucity of literature on healthcare transition for adolescent and young adults with type 2 diabetes. Although many of the medical and psychosocial issues for healthcare transition may be similar for adolescents and young adults with either type 1 or type 2 diabetes [8], it is also important to consider how the unique aspects of type 2 diabetes (e.g., social stigma, comorbid complications) should be addressed in future healthcare transition interventions. In addition, given the increasing prevalence of type 2 diabetes diagnosed during childhood or adolescence [24], adult diabetes providers need to be aware of potential differences between individuals with type 2 diabetes who were diagnosed prior to their transition to adult care versus those individuals who were diagnosed with type 2 diabetes in adulthood [25]. However, no transition intervention models specific to type 2 diabetes exist in the literature to date.

Turner Syndrome

Adolescence can be an especially difficult time for girls and women with Turner syndrome both medically (e.g., estrogen therapy) and psychosocially (e.g., social skills deficits, anxi-

ety) [26]. Therefore, Turner syndrome clinical practice guidelines recommend a planned and staged healthcare transition for patients with Turner syndrome starting in early adolescence [27]. This is an ideal time to promote increased self-care skills as well as raise awareness of future health risks, through prevention and screening for common adult conditions often associated with Turner syndrome (e.g., type 2 diabetes, cardiac issues, and osteoporosis). Since as many as 30% of young women with Turner syndrome lack medical follow-up [28], newer healthcare transition models need to utilize both the general tools (<http://www.gottransition.org/providers/index.cfm>) as well as Turner syndrome-specific tools (e.g., anticipatory guidance for relevant adult conditions) to try to ensure a more successful healthcare transition.

Patients with Turner syndrome cope with many endocrine, genetic, cardiovascular, developmental, reproductive, and psychosocial issues [26]; therefore, their healthcare transition should be completed by a team of Turner syndrome specialists to address the complex nature of this syndrome. Two types of healthcare transition models that are common in Europe and in a few locations in the United States [27] are (1) centers of excellence in which all subspecialty care occurs as part of one large clinic visit in one physical clinic location (same health system, same providers; see Table 3.1) and (2) comprehensive centers in which adult-based providers (usually an endocrinologist and a Turner syndrome care coordinator) network with subspecialty consultants in the same health system and become the “medical home” for the patient with Turner syndrome (same health system, new providers; see Table 3.1).

The University of Florida’s Turner Syndrome Center of Excellence allows for consolidated care to occur by having the same pediatric multidisciplinary team (endocrinology, cardiology, psychology, and nutrition services) provide all the medical care throughout the healthcare transition (same health system, same providers; see Table 3.1). There are many advantages to this model because the specialists have a high degree of knowledge about the adolescents and young adults and it does not require patients to change providers or

healthcare systems [29]. Second-tier specialists (e.g., audiology, genetics) also participate in clinic visits as needed, so that all their patient's medical and psychological needs are met. However, these appointments may take up to an entire day for patients and require a large healthcare system with access to many subspecialists who coordinate their time together based on the individual transition needs of patients.

Alternatively, the Cincinnati Children's Hospital Comprehensive Turner Syndrome Clinical and Research Center becomes a "medical home" during the healthcare transition (same health system, new providers; see Table 3.1) where the core Turner syndrome team is comprised of both pediatric and adult endocrinologists, social workers, dietitians, and a nurse care coordinator. The nurse care coordinator not only helps the patients navigate various subspecialty referrals (e.g., cardiology, psychology) throughout their life span but also become more of a transition coordinator, who provides tailored transition readiness assessments and education to each adolescent and young adult. They can also be a consistent presence as the adolescent and young adult's healthcare transition from their pediatric to adult provider within the same health system. This model is very patient-centered, and medical care is tailored to that adolescent and young adult's individual needs but works best in a large healthcare system and requires excellent communication across the various subspecialties who are all treating the adolescents and young adults separately.

Not all young adults with Turner syndrome have access to integrated pediatric-adult multidisciplinary care programs and will have to be transitioned to adult care that is distinct from their previous pediatric specialty care. A successful healthcare transition from pediatric to adult care can still occur in these settings, as long as the process utilizes the elements outlined in the clinical practice guidelines [27], a "transition champion" is identified to oversee transition activities, and a concerted effort is made to establish a good partnership with the receiving adult provider (including good interprofessional communication strategies). However, more empirical

evidence is needed to determine the medical and psychosocial outcomes of these distinct types of healthcare transition models for adolescents and young adults with Turner syndrome.

Congenital Adrenal Hyperplasia

Pediatric endocrine care for congenital adrenal hyperplasia (CAH) is delivered through subspecialty service, and clinical guidelines recommend that adolescents and young adults with CAH remain in subspecialty services through healthcare transition and as adults [30]. However, studies suggest that as few as 2–5% of individuals with CAH attend subspecialty adult services [31] indicating that improvements in the healthcare transition process are needed. Many international groups have suggested that patients of all ages with CAH are best managed by multidisciplinary teams given their unique endocrine, genetic, reproductive, and psychosocial needs. Joint pediatric-adult care models (same or new health system, same and new providers; see Table 3.1) including pediatric and adult endocrinology providers, at a minimum, are recommended to optimize communication during the transfer from pediatric to adult care, although controlled studies examining transition approaches are lacking [32]. Two research groups used convenience samples to compare adolescents and young adults with CAH who participated in tailored transition programs to those who did not, but the results were not promising. In the first study from the UK, the introduction of a “young person clinic” (i.e., pediatric and adult endocrine teams, along with urology, gynecology, and psychology support as needed) did not improve continuity of care following the healthcare transition to adult specialty care [32]. In the second study from France, self-reported quality of life did not differ between patients who participated in one of four different adolescent and young adult transition programs across different sites and those who did not [33]. Since specific information about the components of these transition programs

was not provided [11], future research on healthcare transition in this population should address these details given the need to establish replicable programs. Nevertheless, both research groups noted that they learned from these initial findings and are working on developing more effective transition programs [32, 33].

Recently published guidelines for Comprehensive Care Centers (CCCs) for CAH resulted in the development of four CCCs in the United States (<https://www.caresfoundation.org/what-we-do/comprehensive-care-centers/>). All CCCs are comprised of multidisciplinary teams that treat newborns, infants, children, adolescents, and adults with CAH and include pediatric endocrinologists, adult endocrinologists, reproductive endocrinologists, pediatric urologists/surgeons, gynecologists, geneticists/genetic counselors, behavioral health professionals, nutritionists, social workers, and nursing staff [34]. Although each CCC has its own approach for transitioning adolescents and young adults with CAH to adult-based care, the guidelines provide specific recommendations for the healthcare transition: (1) initiation of the transition process well in advance of the change in healthcare providers; (2) individualizing a transition plan; (3) facilitation of referrals to adult specialty providers; (4) timing of the transfer of care between ages 16 and 21 with the exact time being a joint decision among the patient, family, and pediatric endocrinologist; and (5) provision of medical records with a summary capturing the patient's essential characteristics, treatment, and needs [34]. As there are no published data on the effectiveness of CCCs, therefore, research examining health and psychosocial outcomes of adolescents and young adults who participate in CCCs for their healthcare transition is needed.

Other CAH experts recommended that adolescents and young adults with CAH achieve these specific knowledge goals as part of the healthcare transition process: (1) understand that CAH is a lifelong disease that is genetically inherited, (2) recognize the medication regimen and consequences of too much or too little medication, (3) be able to self-

manage stress doses of glucocorticoid during illness, (4) knowledge of surgical history and physical implications, and (5) appreciate infertility risks but also that fertility and satisfying sexual experiences can still be achieved [35]. Since these knowledge goals were specified based on expert consensus, research examining the health and psychosocial outcomes of adolescents and young adults who achieve these goals during the healthcare transition would be beneficial.

Although not all adolescents and young adults with CAH will have access to joint pediatric-adult care clinics or CCCs, it is still possible for providers treating this population to implement some of their structured transition program components. For example, providers can work with patients and families to establish a transition plan well in advance of the transfer of care, assist adolescents and young adults in achieving knowledge goals, provide referrals to other specialty care providers (e.g., behavioral health specialists), and establish partnerships and/or means of communicating with receiving adult providers. With this in place, it is more likely that adolescents and young adults with CAH will successfully establish care with adult providers and improve or maintain their health status and quality of life.

Endocrine Sequelae of Childhood Cancer

Few clinical programs specifically address the transition of endocrine care for adolescent and young adult survivors of childhood cancer, but the pediatric oncology literature contains numerous descriptions of transition programs in general [36]. The healthcare transition for adolescent and young adult survivors of childhood cancer is complicated by the fact that late effects are diverse and can include a range of different diseases and psychosocial problems, each requiring the expertise of subspecialists and other healthcare professionals [37]. Three general healthcare transition models for adolescent and young adult survivors of childhood cancer have been described in the literature [38]. First, the cancer center-

based model is an integrated model in which pediatric and adult care occurs within the same governing institution and involves direct collaboration between the pediatric oncology team and adult care subspecialty providers, including endocrinologists (i.e., same health system, new providers, or joint pediatric-adult care; see Table 3.1). Second, the community-based and hybrid models require integration of the adolescents and young adults into adult care in a new health system, usually to a primary care physician, who provides referrals to subspecialty healthcare providers, such as endocrinologists on an as-needed basis (i.e., new health system, new providers; see Table 3.1). The hybrid model also offers primary care physicians ongoing consultation with the pediatric cancer treatment center [36]. Finally, some pediatric cancer centers provide “tiered care” to adolescent and young adult cancer survivors based on their long-term risks and psychosocial needs, such that the cancer-center based model is followed for higher-risk patients and the community-based or hybrid model is followed for lower-risk patients [39, 40]. The Focus Under Forty Program, developed through a partnership between the American Society for Clinical Oncology University and the LIVESTRONG Foundation, offers primary care physicians educational materials for providing transition care to adolescent and young adult survivors of childhood cancer [40]. Another novel and promising version of the hybrid healthcare transition model is through the use of telemedicine to connect patients and primary care physician dyads to a pediatric cancer survivorship team provider during appointments who provides screening and surveillance recommendations for potential late effects [41].

Rather than the pediatric cancer centers taking the lead on the healthcare transition for adolescent and young adult to adult care, some centers in Europe rely on adult endocrinology providers as the lead provider (i.e., new care system, new provider) given the pervasiveness of endocrine late effects. For example, the Transition Unit for Childhood Cancer Survivors at the San Giovanni Battista Hospital of Turin (Piedmont, Italy) is a transition clinic led by an adult endocri-

nologist, who provides referrals to other adult specialists as needed. Adolescent and young adult survivors are typically transitioned to this clinic when they are over 18 years old and off-therapy for at least 5 years [42]. A retrospective study of adolescents and young adults followed in this transition clinic indicated that over half had at least one endocrine late effect and detailed the risk factors contributing to the development of these symptoms (i.e., male sex, radiation therapy, hematopoietic stem cell transplantation, and older age at cancer diagnosis). However, there was no research examining the impact of specific components of the transition clinic on the health and psychosocial outcomes of these adolescent and young adult cancer survivors.

Another similar model where the adult providers lead the healthcare transition for adolescents and young adults is the Late Effects Clinic of the Department of Oncology at Skane University Hospital (Lund, Sweden). Specifically, all adolescent and young adult childhood cancer survivors who are treated with cranial radiotherapy and total body irradiation are referred to an adult endocrinology clinic. In this clinic, survivors are tested and treated for endocrine disorders and also receive care coordination, including psychosocial support and referrals to other subspecialty providers, through an endocrine nurse coordinator [43]. A qualitative study examining outcomes from the Late Effects Clinic indicated that the clinic increased adolescents and young adults' understanding of late complications which improved their self-confidence, assisted with overcoming issues related to employment and health insurance, and provided confidence in, and appreciation of, the healthcare they received [23]. Additional research examining the long-term health and psychosocial outcomes of adolescents and young adults who are followed in the Late Effects Clinic is still needed.

Regardless of the specific healthcare transition model followed, several clinical needs should dictate the services provided to adolescent and young adult survivors during the healthcare transition, including management and detection of late effects, support of psychosocial functioning, provision of

health education, and assistance with financial issues [36]. Additionally, all healthcare transition models should abide by the following principles to help adolescent and young adult cancer survivors achieve a successful healthcare transition: (1) the healthcare transition should be a process rather than a discrete event; (2) the healthcare transition process should be initiated well in advance of the actual transfer of care; (3) healthcare responsibility and participation in medical decision making should be a gradual process based on the developmental readiness of the patient; (4) a specific transition plan should be developed for each survivor beginning at least 12–18 months before the planned event; and (5) as part of that transition plan, viable options for continuance of health insurance coverage should be explored [36]. Thus, the best healthcare transition models are those that effectively address these needs and principles while also accommodating available resources [36].

Transgender Care

One of the primary medical interventions for adolescents and young adults who receive transgender care is the suppression of puberty and promotion of cross-gender secondary sexual characteristics for their affirmed gender through hormone therapy (e.g., estradiol, testosterone) [44]. Therefore, the Endocrine Society Clinical Practice Guidelines outline the recommendations that both pediatric and adult providers receive appropriate training in hormone therapy before providing transgender care to individuals [45]. They also recommend that within this population there is an integration of both medical interventions (e.g., hormone therapy) and mental health evaluations (including mental health interventions, if warranted).

When working with adolescents and young adults who receive transgender care, it is important to have a strong multidisciplinary team who all adhere to a similar treatment protocol [46], including specialists in endocrinology, mental health services (e.g., assessment, therapy, family/parental support, and advocacy), gynecology and urology, speech therapy,

and surgery [47]. Some multidisciplinary medical centers exist in both Europe (e.g., the Netherlands) and the United States [e.g., Boston Children's Hospital (Gender Management Services), the University of California, San Francisco (Child and Adolescent Gender Center Clinic at Benioff Children's Hospital), the Transgender Health Program of St. John's Well Child and Family Center in Los Angeles, and the Transgender Health Clinic at Cincinnati Children's Hospital Medical Center]. However, many of these centers are housed within children's hospitals and only serve individuals through young adulthood (i.e., around 24 years of age); therefore, less is known about appropriate healthcare transition models in this population.

Given the health risks associated with hormone therapy (e.g., hypertriglyceridemia and polycythemia) and the potential for long-term health complications (e.g., cardiovascular disease and osteoporosis) for those who receive transgender care during adolescence and young adulthood, the World Professional Association for Transgender Health (WPATH) Standards of Care highlights the importance of the healthcare transition to an adult provider to provide lifelong care [47]. Although pediatric endocrine specialists may be crucial for individuals who are actively receiving transgender care to achieve their affirmed gender during adolescence and young adulthood, subsequent adult healthcare (e.g., screening for comorbidities associated with the individual's natal sex and management of long-term hormone use) may be best provided through adult primary care. However, adult primary care providers still need to obtain the necessary knowledge and experience to be familiar in caring for adults who received transgender care [48] and/or become more comfortable in co-managing/consulting with other providers who specialize in hormone therapy through participating in initiatives with WPATH, the Endocrine Society, or other national organizations [47]. This way, primary care adult providers can deliver broad healthcare services, beyond maintenance of hormone therapy alone, in one setting to an adult population that is often medically underserved.

The pediatric multidisciplinary specialists have a unique role in providing transgender care (e.g., pubertal suppression and initiation of hormone therapy) for adolescents and young adults to achieve their affirmed gender. In addition, the adult primary care provider also has a crucial role in ensuring life-long medical follow-up for individuals who receive transgender care (e.g., maintenance of hormone therapy and management of adult comorbidities). Given that many transgender clinics only provide services to adolescents and young adults until the age of 24, the healthcare transition model for this population, by default, most often follows the new health system, new provider approach (see Table 3.1). Little is known about the medical and mental health outcomes based on this healthcare transition approach from pediatric to adult care providers for adolescents and young adults receiving transgender care, but there is some evidence in the general transgender care literature, which suggests that interventions that promote family support and anticipate potential lags in parental acceptance may serve as a protective factor for negative psychological outcomes [48]. More research is warranted in determining what outcomes should be measured to indicate a successful healthcare transition as well as what specific clinical interventions may have a positive impact on healthcare transition in this population.

Summary

A review of the literature on four healthcare transition models has been provided, which includes a discussion of a wide variety of structured transition program approaches for six endocrine conditions (i.e., type 1 and type 2 diabetes, Turner syndrome, CAH, childhood cancer, and transgender care). Although still in the early stage of development, the literature in the field of clinical implementation revealed an impressive array of clinical strategies aimed to address the multiple barriers associated with healthcare transition for adolescent and young adults with various endocrine condi-

tions. However, few centers have both implemented and sustained comprehensive healthcare transition programs for adolescents and young adults with endocrine conditions. Indeed, the literature is largely limited to review articles and descriptions of potential healthcare transition methods or to clinical studies where the healthcare transition intervention outcomes examined often lacked comparison groups. Moreover, there have been almost no randomized controlled trials of healthcare transition interventions in these populations [23]. Additional research is needed to determine the key components of effective healthcare transition programs and interventions for adolescents and young adults with endocrine conditions before they can be widely adopted by clinics. Even though the specific approaches through which the adolescents and young adults may transition to adult care is still quite varied across clinic settings, the core elements needed for a successful healthcare transition process are well accepted (e.g., individualized transition preparation planning, tailored anticipatory guidance, healthcare navigation tools, and transfer completion practices/communication). Therefore, the structured transition programs described in this chapter should be further validated empirically in order to determine what best meets the needs of the various adolescent and young adult endocrine subpopulations.

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Chapter 4

Pediatrics: Practical Considerations for the Transition Process



Courtney N. Sandler and Katharine Garvey

Introduction

Among the many issues pediatric providers and healthcare systems face in caring for young adults with chronic illness, determining when and how to effectively transition adolescents to adult practices offers a unique set of challenges. Multiple studies have shown that ineffective transition of care can lead to gaps in healthcare delivery and ultimately loss to follow-up for patients with chronic endocrine conditions such as type 1 diabetes [1–3], congenital adrenal hyperplasia (CAH) [4, 5], Turner syndrome [6, 7], and cancer survivorship [8–12], with the potential consequence of worsening health outcomes.

A seminal general pediatrics paper by Reiss and colleagues in 2002 provided early evidence of these key transi-

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tion challenges as voiced by pediatric healthcare providers as well as young adults with special healthcare needs and their parents. Integral themes included mourning the loss of an often lifelong relationship with pediatric providers, fear that adult providers will be ill-equipped to deliver the same quality of care, changes in health insurance status, and concerns over the continued role of families/caregivers in the care of the young adult patient [13]. These themes have since been echoed in the pediatric endocrinology transition literature [1, 5, 7, 12, 14, 15], including documentation highlighting specific challenges related to care delivery fragmentation and suboptimal transition preparation.

This chapter focuses on practical recommendations to support pediatric endocrinology providers in providing transition care, drawing from professional guidelines and resources in general pediatrics and pediatric endocrinology as well as published literature in type 1 and 2 diabetes, CAH, Turner syndrome, and cancer survivorship as exemplars of chronic endocrine disorders. While there is no published literature in the transition to adult care for transgender young adults, recommendations are likely relevant.

Practical Recommendations for Pediatric Transition Care

Consensus Guidelines and “Got Transition”

The transition process includes planning and preparation, coordinated transfer to the adult care system, and intake into the adult care system. The importance of these steps has been repeatedly recognized by expert consensus statements. For a general approach applicable to all patients with chronic medical conditions, providers can look to the expert consensus transition guidelines put forth by the American Academy of Pediatrics (AAP), American Academy of Family Physicians, and the American College of Physicians in 2011 [16]. A European expert panel published specific guidelines encom-

passing transition care for childhood-onset growth hormone deficiency, Turner syndrome, Prader-Willi syndrome, and cancer survivors, with detailed medical as well as care coordination considerations for these populations [17]. Specific to type 1 diabetes, a position statement of the American Diabetes Association, in collaboration with many professional societies, detailed diabetes-specific recommendations for transition preparation and coordination [18]. In the United Kingdom, the National Health Service recently published Diabetes Transition Service Specification to emphasize early preparation, pediatric interventions to facilitate a smooth and coordinated transfer, and support of integration into adult care settings [19].

The US “Got Transition” initiative [20] provides extensive online transition resources freely available for use by health-care providers, patients, and families, all of which reflect the latest expert consensus recommendations. These resources are structured around six core practice elements that comprise an optimal approach to transition based on current best practices, including establishing a policy, tracking progress, administering transition readiness assessments, planning for adult care, transferring, and integrating into an adult practice. While these recommendations were developed as a general approach to transition, the structured approach of “Got Transition” is readily adaptable to endocrinology practices, in which patients often have chronic multi-organ system surveillance and management needs requiring care coordination.

A Roadmap for Transition Care

Figure 4.1 summarizes the key steps to optimize transitions for patients with chronic endocrine conditions, guided by synthesis of the literature, transition resources, and consensus statements. The outlined steps are each discussed in further detail below, including *setting expectations*, *transition preparation*, *transfer coordination*, and *transition tracking*. Each of these steps is discussed below, with a focus on the preparation and coordination steps essential to the pediatric provider role.

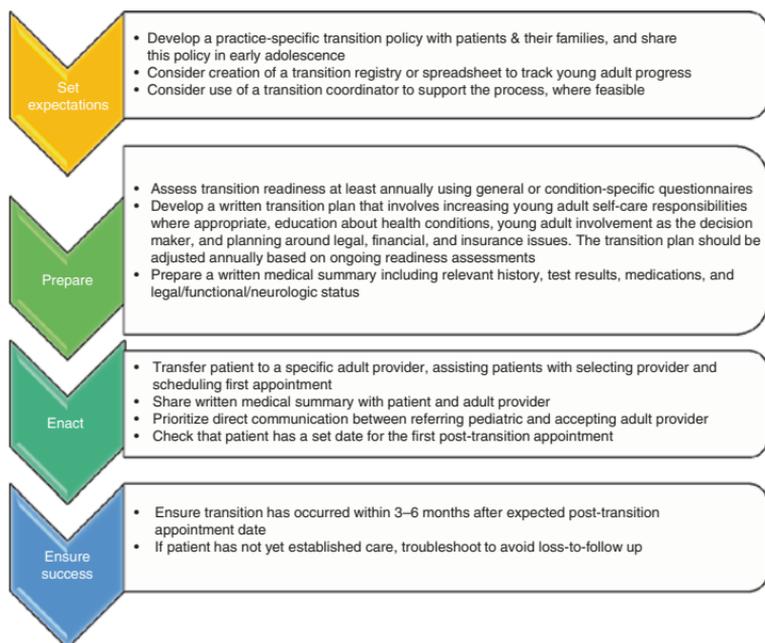


FIGURE 4.1 Key steps to support optimal transition of care for patients with chronic endocrine conditions

Setting Expectations

It is critically important to ensure that patients and families learn early on what healthcare transition is and what to expect in the future. The type 1 diabetes literature offers key insights to facilitate understanding of patient and family preferences in transition care. These preferences include a desire for the transition conversation to start at an earlier age, a desire for providers to acknowledge developmental challenges and competing life demands, and a desire for parents to remain in a support role even as patients take on more independence [21–23]. Emotional attachment to pediatric providers has also been identified as a major barrier to transition planning and transfer to adult care [1, 23, 24]. Given these factors, setting clear expectations will help to psychologically equip patients, families, and providers for the transition process.

The first step toward expectation setting in pediatric endocrinology practices involves the development of a practice-specific transition policy statement. A number of key stakeholders should contribute to the creation of this policy, including providers, staff, patients, and families/caregivers. Sample transition policies are available through “Got Transition” [25]. In general, the following should be clearly stated:

1. *The goals of transition.* Examples include promotion of autonomy and self-care where possible, acquisition of condition-related knowledge and skills, and well-coordinated transfer of care from pediatric to adult care services, when appropriate.
2. *The expected age or developmental stage for transition at the practice.* Note that there is no clear consensus in the literature or by professional societies regarding the age or developmental stage transition policies should set for the transfer to adult care and current practice patterns are highly variable. A study of 185 young adults with type 1 diabetes and a similar study of 182 young adults with type 2 diabetes followed from adolescence in the SEARCH for Diabetes in Youth study found that for those who had transitioned to adult diabetes care compared to those still receiving pediatric care, the odds of poor glycemic control at follow-up were 2.5 times higher in type 1 diabetes and 4.5 times higher in type 2 diabetes [26, 27]. Similarly, in a study of 118 youth during their senior year of high school and 1 year later, those who remained in pediatric care had significantly less deterioration in glycemic control [28]. These studies suggest that pediatric care may be more developmentally appropriate and supportive for the early young adult population, but further research and consensus are needed in type 1 diabetes as well as in other endocrine disorders. Further, current institutional or national policies may dictate a particular transition age (e.g., 18 years in many areas), and patient neurocognitive status and legal status are also critical considerations. While there is no established best practice regarding transition age,

delay of transition based on the developmental needs of the patient may be appropriate, where possible.

3. *The practice's transition planning approach.* Recommendations for transition preparation are discussed in detail below.
4. *The roles/responsibilities of patients, caregivers, and the medical practice in the transition process.* Studies in type 1 diabetes suggest that families prefer for parents to remain in a support role even as patients take on more independence [21–23]. Similarly, a recent qualitative study of Latino young adult cancer survivors revealed the importance of the nuclear family in follow-up care [29].

The completed transition policy should be disseminated throughout the practice to employees at all levels to ensure that appropriate resources are in place. The policy should also be given to patients and their families in early adolescence. In general, professional organizations recommend the introduction of the transition policy to patients and families between the ages of 12 and 14 years. The policy should also be available for ongoing review by patients and their families throughout the transition process.

In order to encourage ongoing transition-related activities, providers should be aware of which patients have received the transition policy. “Got Transition” advocates the creation of a registry of young adult patients who will be going through the process of transition. Receipt of the transition policy may signal entry into this registry. Flowsheets incorporated into the registry can be used to keep track of where patients are in their transition process, from the time they are introduced to the transition policy up until hand-off to an adult provider. Registries and flowsheets may be useful in ensuring that the stages of transition, as described in this chapter, have been met.

Transition Preparation

Pediatric transition preparation is the central component of the transition process, but a number of studies from different healthcare systems have shown deficiencies in transition prep-

aration. Providing examples from the type 1 diabetes literature, more than half of 101 post-transition patients in a German study reported negative transition experiences, including lack of transition preparation [14]. In a recent national US sample from the Type 1 Diabetes Exchange, two-thirds of post-transition young adults felt mostly or completely prepared for transition, and many had not received counseling in key transition preparation topics [1]. Along similar lines, in Australia, a recent chart review study showed that one-third of transitions occurred in an unplanned way or without adequate physician input, record transfer, or sign-off [30].

All stages of transition preparation, as outlined below, may be facilitated by collaboration from multidisciplinary team members in addition to pediatric endocrinologists – including nurses, social workers, psychologists, care coordinators, and financial counselors.

Readiness Assessment

The first stage of transition preparation involves the completion of an assessment of transition readiness. Both the AAP and “Got Transition” advocate an initial transition readiness assessment starting in mid-adolescence, with reassessment annually. These assessments allow providers to identify areas of strength and weakness to be used toward ongoing education and support of increasing patient self-care independence. Both patients and caregivers should be encouraged to contribute helpful information regarding the youth’s readiness to transition. The results of initial and annual assessments can be incorporated into patient registries and flowsheets to track young adult progress.

1. Available general transition readiness assessment instruments (not specific to any condition) include:
 - The *Transition Readiness Assessment* through “Got Transition” is a one-page form to be filled out by the patient, with help from parents/caregivers as needed. As a general assessment of transition readiness, two ten-

point scales evaluate (a) how important transition is to young adults as well as (b) their overall confidence in preparation for adult care. Simple yes/no questions assess a young adult's personal health understanding and skills in healthcare engagement in order to highlight specific practical areas of improvement to patients, parents/caregivers, and providers [31].

- The *Transition Readiness Assessment Questionnaire (TRAQ)* is a tool validated in youth with special health-care needs, which asks patients and/or their parents/caregivers to assess their current level of engagement in self-management and self-advocacy skills. Responses highlight areas where transition readiness can be improved and provide insight into exactly where in the self-care spectrum patients are with certain skills [32].
 - The *STARx Questionnaire*, also validated in chronic disease populations, is another self-assessment tool that measures readiness in domains of knowledge, communication with provider, and self-management on a five-point Likert scale that can then be used to provide transition readiness scores in each domain [33].
 - The *Am I on TRAC-For Adult Care Questionnaire* also uses a Likert scale to assess knowledge and behavioral indicators of transition readiness. Scores are tallied according to a threshold, above which a young adult can be considered ready for transition to adult care [34].
2. In addition to the generalized tools above, condition-specific readiness assessment tools are available through the Endocrine Society. These were also developed via expert consensus and include:
- The “Type 1 Diabetes Skills Assessment,” which is completed by the patient's diabetes providers. Providers indicate when patients have demonstrated certain basic knowledge of diabetes, mastery of diabetes management skills (including the use of technologies), medical care logistic management, and emergency diabetes management [35].

- The “Turner Syndrome Transition Readiness Assessment,” also completed by pediatric providers, assesses health understanding and skills in healthcare engagement and includes a section on social/emotional factors related to transition [36].
- The “Growth Hormone Deficiency Assessment of Patient Skills,” also completed by pediatric providers, includes knowledge and skills-based assessment and is applicable to other pituitary hormone deficiencies (including sections pertinent to adrenal insufficiency, diabetes insipidus, hypothyroidism, and sex steroid replacement) [37].
- In addition to readiness assessments, the Endocrine Society transition resources for type 1 diabetes and growth hormone deficiency also include additional questionnaires for “Patient Self-Assessment of Worries, Concerns and Burdens Related to Transition,” in which the patient is asked about the presence of various issues related to care burden, mental health, and transition preparation/readiness in a yes, maybe, or no format, with free space to record any unique concerns. The acknowledgment of any issues provides possible areas for provider intervention.

Self-Care Education

Transition preparation should also include ongoing education of the young adult about their health condition. In many conditions, early adulthood may be the time in the natural history of disease in which complications first manifest. This is particularly true for disorders such as type 1 diabetes and Turner syndrome, in which tools for providers to assess patient knowledge are available as previously discussed. In the cancer survivorship population, the need for improved education of young adults is vital to transition success. As many patients have not manifested any signs of late adverse health effects at the time they are expected to transition care and may not be aware of the risk of late effects, they are less likely to engage

in care with adult providers [9]. For instance, a 2016 study by the Swiss Pediatric Oncology Group found that of 465 survey participants, only 56% remained in survivorship care, the majority of whom (80%) believed their susceptibility for late effects was low. Those who believed follow-up care was not necessary were less significantly less likely to continue to engage in care [38].

The young adult patient should be involved in medical decision-making, as appropriate from a neurocognitive standpoint. Tips for self-care, care management, and self-advocacy are available through “Got Transition.” In addition, to help the young adult keep track of providers, pharmacies appointments, questions for providers, and health concerns, a blank “health diary” is available from the Pediatric Endocrine Society, developed by Connecticut Children’s Hospital [39].

Transition Plan

When deemed appropriate following readiness assessment, likely around the age of 16–17 years, an individually tailored transition plan should be developed in collaboration between patients, families/caregivers, and providers and reviewed annually. This plan should be formally written, provided to the patient and family, and ideally entered into the patient’s electronic health record and transition registry. The plan should address a process for the patient and their family to achieve longitudinal, realistic goals toward reaching maximal independence. It should also outline the roles and responsibilities of the patient, provider/practice, and family/caregiver. These may include the patient gradually increasing self-care responsibilities such as scheduling appointments, obtaining medications and/or supplies, administering medications, and having one-on-one interactions with the medical provider.

Practical concerns should also be addressed as part of the transition plan, such as financial and insurance concerns. For example, in an analysis of the potential factors associated with young adult engagement in adult-oriented cancer follow-up care, disease and treatment-related vari-

ables such as cancer severity and treatment intensity were not associated with care engagement, while lack of health insurance was identified with decreased follow-up care [33]. Other issues to be considered in transition planning include changes in consent and legal decision-making, which may be particularly important for youth with neurocognitive deficits. A 2017 survey of pediatric oncologists in the US Children's Oncology Group identified perceived cognitive delay and social challenges as barriers to effective care transition [40]. Patients and families should be directed to resources to address these issues. Where available, information for condition-specific support groups should be given to patients and their families given the power of peer support to troubleshoot issues and encourage ongoing condition-related care [6].

Medical Summary

During the transition planning phase, a written medical summary should be prepared and provided to patients and caregivers, including diagnoses, prior treatments and procedures, the result of recently completed disease-specific surveillance exams, medication reconciliation, and, where applicable, the documentation of legal, functional, and neurologic status. This document should be updated as part of ongoing transition assessment and planning annually and eventually be routed to the adult provider at the time of transfer.

Sample medical summaries for patients with type 1 diabetes, Turner syndrome, and growth hormone and other pituitary hormone deficiencies are available in the bundle of transition resources from the Endocrine Society [35–37]. Similarly, the team at Connecticut Children's Hospital has created “transition passports” for patients with Turner syndrome, childhood cancer survivors with endocrine late effects, and patients with pituitary or other endocrine disorders that can be found on the Pediatric Endocrine Society website [41]. These passports include many sections relevant to the pre-transition patient, including general sociodemographic and

insurance information, sections for relevant medical history and recent laboratory tests, targeted risk assessments for various related comorbidities, psychosocial risk assessments, and a section on life goals. The passports end with information relevant to the patient about to transition including names of specific referrals and recommendations for adult surveillance care. Therefore, they are intended for use by patients and their families as well as both pediatric and adult providers.

Transfer Coordination

Once a patient has achieved their readiness goals, at the decided-upon time, the pediatric team should implement the plan to transition to an adult provider. Deficiencies in transition coordination and referrals to adult care have also been highlighted in the type 1 diabetes literature. In a single-center US study of 250 post-transition young adults, only half of respondents received specific adult provider or clinic recommendations [2], and in the more recent national US sample from the Type 1 Diabetes Exchange, two-thirds of post-transition young adults reported receiving an adult provider recommendation or contact information prior to transition [1].

Thus, it is critically important that the patient receive a *targeted* referral to a *specific* adult medical provider, who may be chosen based on specialized knowledge base, patient-provider personality fit, geographic location, and/or acceptance of patient's insurance. The provider may also be chosen based on resources at the accepting adult facility, as patients with complex endocrine disorders may require multiple subspecialists and benefit from having all of their care in one institution. Depending on availability, varying models of care suggest a face-to-face introduction to the adult provider, a joint "transition" appointment, or simply the provision of contact information and assistance with first appointment scheduling.

Of note, an administrative or transition coordinator support may be particularly helpful in supporting these referral

and coordination tasks. In the type 1 diabetes literature, transition navigators have been associated with more frequent follow-up and reduced gaps in care in Canada [42] and improved glycemic control and fewer diabetes-related hospitalizations in Australia [43]. Clinical programs may consider implementing transition coordinators where possible, but this approach is also associated with increased costs that may not be feasible for many programs.

Direct communication between the pediatric transferring provider and accepting adult provider is another important factor, particularly in the case of patients with complex needs. In fact, provider studies from both pediatric and adult endocrinologist perspectives in type 1 diabetes have pointed to existing suboptimal pediatric transition preparation practices and the need to increase frequency of direct communication between pediatric and adult providers for patient hand-offs [44–46]. The transition summary that has been prepared as part of the transition planning process should be signed by both the pediatric provider and the patient/family, with copies provided to the patient/family and receiving adult provider and direct communication follow-up by the pediatric provider.

Some groups advocate a certificate of graduation for patients who have completed their final pre-transition visit as an acknowledgment of the hard work of going through transition and as a physical reminder of their upcoming commitment to transition. This certificate should include the patients' name and recognize them as a graduate of their specific pediatric provider, moving onto healthcare with their specific adult provider [6, 13].

Post-transition Tracking

After transfer, the pediatric provider should remain available for patients in order to address specific issues such as incomplete records or to address any questions about the patient's history. Ideally, within 3–6 months after the final pediatric visit, the pediatric practice should ensure that the patient had their

first adult provider appointment in order to close the loop and prevent gaps in healthcare delivery. This is the area in which a patient transition registry can be particularly useful, to ensure any patients who have initiated the process have successfully moved into adult care. This will also allow the pediatric provider to be alerted to any issues with the transfer and to strengthen relationships with adult centers to whom they refer patients.

The potential value of transition tracking is highlighted by data from the CAH literature. A retrospective study of transition practices in the United Kingdom tracked 61 patients with CAH; 50% of these patients were lost to follow-up. Patients who did not attend one of their first two post-transfer appointments (“poor early attenders”) were more likely to be lost to follow-up, as were those with worse pre-transition control. This study suggests that CAH patients failing to optimize their healthcare in adolescence and engage in early post-transition care may be more likely to experience gaps in care delivery and poor disease control as adults. Interestingly, a similarly high rate of loss to follow-up occurred even in patients participating in a planned transition service jointly staffed by pediatric and adult endocrine providers [5]. Deeper understanding of barriers and design of initiatives to improve gaps in care may be elucidated by data from transition tracking registries.

Conclusion

As young adults with chronic endocrine disorders face competing life demands, decreasing parental support, and fragmented medical care, adherence to self-care behaviors often declines, and health outcomes may be adversely affected. Healthcare transition plays an integral role in ensuring continuity of care delivery and adequacy of self-care skills across this vulnerable period. Transition is considered to be successful when an emerging adult demonstrates the ability to adhere to their care plan, coordinate care logistics, and meet with the healthcare team at recommended intervals.

Review of published literature and resources in the field of endocrine transitions points to a number of common themes, including the need for purposeful transition preparation counseling by pediatric providers beginning in adolescence (incorporating education on disease knowledge, self-care, and care coordination skills); the need for planned transfers to adult care (with specific referrals, records transfer, and communication between pediatric and adult teams); and discussion about attachment between patients and pediatric providers and differences between pediatric and adult care.

Existing transition consensus guidelines and resources reinforce these important themes and offer resources for pediatric endocrinology providers and clinical programs seeking to improve transition care delivery and tailor recommendations to specific clinical settings. Given the time constraints on patient-provider visits in pediatric endocrinology, transition coordination programs and multidisciplinary collaborations may be particularly helpful in achieving these goals.

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Chapter 5

Adult Care: Practical Considerations for Patients with Endocrine Conditions Transitioning from Pediatric to Adult Care

Shivani Agarwal

Differences Between Pediatric and Adult Care

Inherent differences exist in pediatric- and adult-oriented care systems. Young adults undergo unique developmental and life changes, which require specific expertise and resources to care for this population [1–3]. Especially in endocrine diseases, which are chronic and require intensive ongoing assessments of disease self-management and multi-disciplinary care [4, 5], certain care paradigms are needed to support and promote health in young adults. Pediatric care is family-centered, is team-based, and often has access to resources of nurses, educational staff, social workers, and psy-

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chologists, which are frequently needed in caring for this population [6–9]. In contrast, adult care is often resource-scarce, lacking adequate staffing of ancillary services and psychological support [6, 8, 9]. Moreover, although recent literature suggests that family or partner-inclusive care is effective for disease control in adults with endocrine disease [10, 11], adult care is still mostly focused solely on the patient, to which young adults may not be accustomed. In pediatric care, the young adult is the center of concentric rings of supportive care while in adult care, the young adult is autonomous and has links to supportive care in a self-directed fashion (Fig. 5.1). The healthcare transition can be particularly challenging for young adults who are not yet ready to change care providers, have not emotionally or developmentally matured, and/or are still dependent on their support systems for many aspects of their care [6, 12, 13].

In addition, the period of young adulthood is an especially vulnerable time for the emergence of psychological comorbidities, including depression, anxiety, suicidal ideation, psychotic disorders, alcohol/drug abuse, and eating disorders [14–17]. Psychiatric disorders, if left unrecognized or untreated, have serious consequences and require support

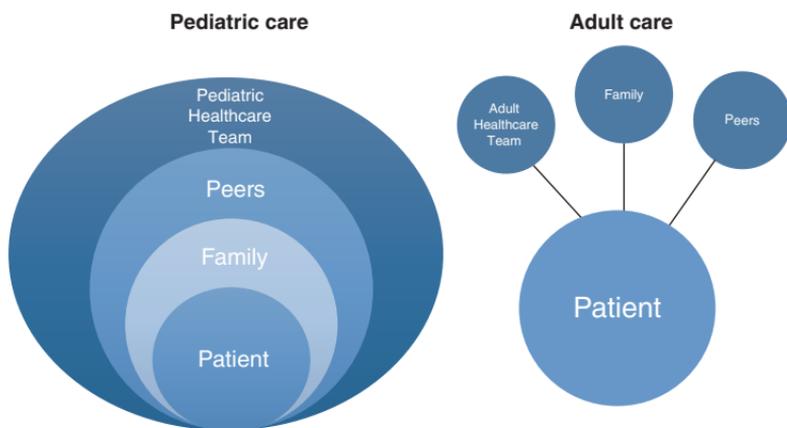


FIGURE 5.1 Patient care paradigms in pediatric and adult care

systems of care. In a study of young adults with type 1 diabetes in the United Kingdom, those with mental health disorders had two times higher risk for recurrent diabetic ketoacidosis and death [18]. In an Australian study of approximately 2000 young adults, 8.5% of the participants who were not in employment, education, or training by age 20.7 years were found to be more likely to have been frequent cannabis users or had mental health disorders as adolescents [19]. Multiple professional societies cite young adult need for appropriate approaches and resources for psychological support to care for their chronic endocrine disease [2, 13, 20], yet these are lacking in adult care more so than in pediatric practices [9, 21].

Adult providers may also not be trained to specifically care for young adults. The data is sparse on this issue, and few studies exist that explore adult provider perspectives on transitional care. In one recent study of adult endocrinologists caring for young adults with type 1 diabetes, they reported feeling ill-prepared to care for this population given increased psychological training needed [9]. Several studies on pediatric provider care perspectives for transgender and CAH individuals reported lack of training in medical and psychosocial issues to care for this population [12, 21], which likely worsens in adult care given general lack of training in these childhood-onset conditions. Training is quite different for pediatric and adult ACGME-accredited US programs, which lead to these provider differences. “Development” and “behavior” are core training areas for ACGME-accredited pediatric residency trainees, whereas adult residency trainees only need “opportunities for experience in psychiatry” [22, 23].

As an added layer of complexity to care resource availability for young adults with endocrine diseases, given the scarcity of endocrinologist nationally [24], many young adults may receive their care from primary care practitioners (PCPs) as opposed to specialists after transferring to adult care. As such, given different levels of exposure and training to specialty endocrine diseases, different care may be deliv-

ered from PCP than specialist. In a recent study which compared training of adult endocrinologists versus PCPs in caring for young adults with type 1 diabetes, adult endocrinologists reported higher levels of training in standards of diabetes care and insulin administration, while PCPs felt more proficient in depression screening and management [25]. These differences in training may have significant consequences for caring for patients with mental health disorders or high-risk behaviors. PCPs may recognize and treat psychiatric disease earlier and have more access to comprehensive services such as social work and psychiatry if they participate in an accountable care organization or medical home model [26, 27]. Specialists may be able to offer more timely advanced endocrine treatments, which could significantly reduce the risk of long-term complications and burden. For example, diabetes technology including insulin pumps and continuous glucose monitors now offers significant advantages over injectable therapies and traditional self-monitoring of blood glucose, thereby reducing disease self-care burden and glycemic control for young adults [28]. Another example includes the use of more nuanced formulations of hormonal therapy in the form of transdermal patches over oral or injectable preparations for transgender patients, which could significantly improve quality of life in this population [21].

In contrast to adult providers, pediatricians may not be specifically trained in diagnosing or managing comorbidities or complications of endocrine diseases which often present in adulthood [2, 12, 13, 29]. For example, in a German sample of approximately 65,000 youth in which overweight and obese status was highly prevalent, 88% had blood pressures documented, but most were inpatient measurements, 67% were screened for dyslipidemia with lipid measurements, and 62% were screened for diabetes [30]. In another example, pediatric providers only started antihypertensive or lipid-lowering medications in youth with type 1 diabetes after persistent elevations or in the setting of additional cardiovascular risk factors, despite endorsing that medications are an effective means for treating hypertension and hyperlipidemia [31].

Overall, issues related to differences between pediatric and adult care can be improved by integrated efforts aimed at several key issues. There must be increased awareness and training of pediatric and adult care providers in the developmental issues, care decisions, and value of multidisciplinary teams (educators, social work, mental health specialists) that impact the delivery of optimal transition care. In addition, structured transition policies need to be developed and implemented in local health systems to help allocate system resources and guide pediatric and adult practices to provide tailored care that meets the unique needs of young adults in transition.

Young Adult Perspectives on Transition Care

Several common themes emerge from published young adult perspectives on transition care and relate to specific domains including (1) timing and readiness for transfer to adult care, (2) expectations of adult care and the quality of the relationship with the new provider, and (3) logistical issues of transferring healthcare systems [2, 12, 13, 32–34].

Regarding timing and readiness for transfer to adult care, young adults are often not prepared in a timely manner, which results in an abrupt transfer as opposed to the recommended gradual transition process [2, 12, 13, 20, 35]. In a study of young adults with type 1 diabetes, young adults who had recently transferred to adult care reported that they did not discuss transition or transfer in pediatric care and wished they had been more prepared for healthcare transition [32]. In addition, both young adults and parents who were about to transition and those who had recently transitioned desired being treated like a young adult in provider interactions and relying on more self-management techniques which put trust in the adolescent or young adult patient [32]. In a study of pediatric endocrinology providers, 45% of participants did not follow a standardized transition process for their type 1 diabetes patients transferring to adult care and 74% endorsed delaying transfer of care due to difficulty ending a longstand-

ing therapeutic relationship [8]. As a result, patients often receive suboptimal preparation for the eventual transition to adult care, which contributes to gaps in care of at least 6 months between pediatric and adult care [32, 34].

Regarding expectations of adult care and the quality of the adult provider relationship, young adults cite mismanaged expectations and poor therapeutic relationships with the new adult provider as an issue in post-transition visit attendance [32, 36]. For example, a qualitative study exploring care utilization and relationships with adult providers for young adults with type 1 diabetes from the United Kingdom revealed that collaborative relationships between young adults and providers increased the perceived value of attendance and reduced barrier burden. Barriers to therapeutic relationships included negative perceptions of diabetes self-management by providers [37]. Similarly, an 18 year retrospective review of a CAH clinic revealed that attendance to the first two adult appointments post-transition indicated overall engagement with adult care and retention in care long-term [12].

Lastly, regarding logistical issues of transfer, independent navigation of the healthcare system is often endorsed as overwhelming by young adults [32, 38]. Management of insurance coverage changes, drug-related costs and logistics of maintenance of refills, and prompt attendance of medical appointments all require a certain amount of financial support/independence, complex decision-making, and executive functioning that are still developing in young adults [1]. Poor handling of these issues could affect health. One study found that 47.5% of youth with type 1 diabetes reported diabetes-related cost and competing priorities as barriers to continued regular ambulatory care [39]. While there is sparse literature on young adult perspectives with other chronic endocrine diseases, young adults with Turner syndrome, transgender, CAH, type 2 diabetes, and endocrine sequelae of childhood cancer likely experience similar logistical challenges as has been described in the majority of chronic childhood diseases [20, 40]. Programs which focus on care navigation and patient education in transition care, such as the use of a health system

navigator to aid in physical transfer of patient and medical documents between health systems and transition preparation educational curricula to better prepare patients for adult care, have demonstrated successful establishment and increased satisfaction of adult care for young adults with chronic endocrine diseases [41–43]. These programs could be generalized to other disease types and tailored to the unique needs of each endocrine disease.

Considerations for Receiving Young Adults into Adult Practice

Understanding the complexity of young adulthood from the patient perspective is paramount in adequately addressing this population's needs in care. In general, young adulthood equates to new freedoms—entering the workforce, moving away from home, and beginning college or starting families; any of these changes complicate the structure required to manage a chronic disease. The transition into adult care is a vulnerable time for these patients due to increased responsibility in self-management paired with decreased structured supports and pressures of balancing competing life priorities.

To start, timely establishment of care for this patient population is vital. Because their chronic endocrine disorders are most commonly diagnosed in childhood, patients may have become comfortable getting care from the same pediatric physician from diagnosis until their entry into adult care. Patients often struggle to navigate the adult healthcare system when they are older, leading to disengagement from their disease management. For those who are not able smoothly establish adult care, they are more likely to report running out of or not being able to afford medication, worse disease control, depressive symptoms, and increased incidence of acute disease exacerbations leading to emergency department visits. Any lapse in care, especially during the vulnerable time period of young adulthood, results in worse clinical outcomes, and the same principle can be applied to other chronic

endocrine disorders. Extra resources on optimal transition timelines and materials are available at Got Transition (<https://www.gottransition.org/>).

Patient perspectives demonstrate that the adult provider-patient relationship is important in perceived successful transition to adult care in the view of the patient [32, 37], as well as increased visit attendance in adult care due to increased engagement in care [12, 37]. Based on intervention work in type 1 diabetes, several adult care practices have been found to be associated with increased satisfaction and engagement in care for young adults transitioning from pediatric care. Figure 5.2 describes a successful transition process model based in adult care [44].

The adult practice may consider developing an individual or group “orientation to adult care” to manage expectations for the incoming new young adult patient and introduce the clinical care team (Fig. 5.2). The author trained staff nurses to deliver the orientation to the patient and their family for 5–10 min after the first visit [44]. These practices were desired by patients in perspective studies [32, 37]. “Care coordination” through confirmation of medical record transfer before the adult visit, frequent follow-up with patients who may be experiencing multiple transitions of care, and ensuring the patient knows how to get to the clinic before the first visit can ease logistical burdens that young adults cite in transition [2, 20, 32, 33]. Examples of transition summary templates exist on the Endocrine Society’s Transitions of Care website (<http://www.endocrinetransitions.org/>). “Pediatric partnership” to identify high-risk patients in transition and ongoing needs to improve self-care or manage other medical problems will not only improve medical care for these individuals but also signal to the incoming new young adult patient that the proper handoff of information was performed. Efforts of “engagement in care” through focusing on building trust at each visit, implementing goal-setting exercises which are self-directed, and checking in during the interim between visits establish the new relationship, improve engagement and can increase retention in care [37, 44]. “Continuing education” providing updated self-care techniques is also key to repair-



FIGURE 5.2 Model of adult-based transition program. (From Agarwal et al. [50])

ing any maladaptive behaviors or practices that are injurious to the patient's self-management of their disease process. Lastly, given how vulnerable young adults are during this period of development, "behavioral support" in the form of formal psychological support or team-based ancillary support should be emphasized by the adult practice to bolster the patient in their new healthcare system and developmental stage. This author coordinates monthly young adult support groups and biannual young adult retreats to foster community among the young adult clinic cohort [44]. In addition to the above adult-based transition care model, adequate office

support for insurance coverage and prior authorizations for specialized endocrine medications need to be offered. Endocrine disorders often require expensive hormones and medical devices to achieve optimal disease outcomes. Taking an active role in overcoming these barriers will bring these young adult patients one step closer to successful disease self-management and prevent lapses in medication administration or loss to follow-up.

Acknowledgment and proper care of accompanying comorbidities are also important. In a recent study, Agarwal et al. found that among an urban young adult-specific type 1 diabetes transition clinic delivered in the adult healthcare setting, 30% of participants had a major psychiatric diagnosis [44]. Studies have found that patients with serious psychological distress have more barriers to achieving optimal disease outcomes than those with chronic diseases [10]. The time and attention required to self-manage any chronic endocrine disorder can be overwhelming, and in the context of a debilitating psychiatric comorbidity, self-management will be nearly impossible without first acknowledging and treating the underlying psychiatric issue. Moreover, the consequences for missing a psychiatric diagnosis in this patient population are serious, with suicide as the leading cause of death in this age group [45]. Psychiatric disease and psychological distress should be screened for at the first appointment, whether or not it was screened for prior in pediatric care. General and disease-specific measures exist, many of which can be used in routine clinical care [46, 47]. In addition to screening for unrecognized psychiatric disease, open non-judgmental conversations about possible risky behaviors will allow these patients to be properly educated and provide opportunities for intervention before complications occur.

It is also critical to screen young adult patients for complications of their disease early. In type 1 diabetes, one in three young adults will have at least one diabetes-related complication or risk-modifying comorbidity by age 21 years [48]. Routine screening during physical exams and visits as well as patient education can mitigate delay of diagnosis

and possible later disability. Discussion of these issues in an open and factual manner can also allow the patient to further process the importance of close adherence to disease management.

A special consideration for females is contraception and pregnancy planning. Thorough assessment of sexual activity, contraception use, past testing for sexually transmitted diseases, and desire for pregnancy should be done early. Unplanned pregnancy could be devastating to disease management if not desired or not accommodated for in the patient's chronic disease care. In CAH and transgender care, certain medications such as exogenous hormone or glucocorticoids could be dangerous early in pregnancy [12, 21]. Additionally, uncontrolled diabetes has been shown to have poor outcomes for mother and fetus [3]. An understanding of patient priorities can create a therapeutic partnership wherein disease control is put in the context of how it relates to these other life goals and responsibilities.

Lastly, addressing suboptimal self-management behaviors in this population in a way that is not isolating but empowering is a unique and critical consideration when caring for young adults with chronic endocrine disease. Although most adult care system structures do not allow for long counseling times in appointments, approaching the patient in a non-judgmental way allows them to create a better therapeutic relationship. Understanding the barriers to poor self-management, which could vary from fear of adverse drug reaction based on pediatric experience to lack of motivation to care for themselves due to underlying burnout or depression, is key to uncover and could improve both their health and effectiveness as a provider [49].

In sum, although current adult healthcare systems are often not structured to support the unique needs of young adults specifically, there are ways to be creative within the current healthcare system in order to care for young adults effectively. Furthermore, there are rewards to reap from caring for this population. By taking the extra time to consider the multidimensional needs of this population, it allows adult

providers to be in the unique position to support, teach, and prepare vulnerable young adults for a lifetime of improved quality of life and increased lifespan.

Conclusion

Young adults with chronic endocrine diseases are a unique and vulnerable patient population. By recognizing the needs of this population and caring for them through the lens of young adult priorities and normative development, health outcomes can be more optimally achieved in an efficient manner. The young adult and transition care approach needs to be tailored and can be accomplished within the current healthcare system paradigm with a creative approach. Ultimately, establishing care pathways for these patients early and taking on the responsibility to establish and nurture a longstanding therapeutic relationship have the potential to prevent early complications and premature mortality.

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Part II
Transition Considerations for
Specific Endocrine Conditions



Chapter 6

Transition Considerations for Youth-Onset Diabetes (Type 1 and Type 2)

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and Jennifer Raymond**

Type 1 diabetes is the most common endocrine condition of childhood, with over 16,000 new diagnoses in US youth each year [1]. Furthermore, the incidence of type 2 diabetes, typically considered a disease of older adulthood, has increased among youth in recent years in parallel with rising rates of childhood

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117

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obesity. Currently, there are over 9,200 new diagnoses of type 2 diabetes among US youth each year, predominantly among adolescents from racial/ethnic minority backgrounds [1]. As type 1 and type 2 diabetes are lifelong chronic conditions, youth with these illnesses need to transition from a pediatric to adult diabetes care provider during late adolescence or early adulthood. This chapter reviews developmental considerations for transition-aged youth with type 1 or type 2 diabetes and provides practical, evidence-based recommendations to support the transition process from pediatric to adult diabetes care. Specific resources to support transition efforts are discussed. As research on transition for youth with type 2 diabetes is still in its infancy, this chapter primarily relies upon studies conducted among youth with type 1 diabetes, with notations made when aspects of these considerations are known to differ for youth with type 2 diabetes.

Developmental and Psychosocial Considerations

Late adolescence and young adulthood is a particularly risky period for youth with diabetes. Among youth with type 1 diabetes, large cross-sectional registry studies report hemoglobin A1c (A1c) is at its highest at age 19 (mean A1c = 9.2%), and as few as 14% of early young adults have an A1c value in the recommended range <7.0% [2]; A1c values among young adults with type 2 diabetes are similar [3]. Complications and comorbidities of diabetes are also prevalent. Representative samples have found that 32% of adolescents and young adults with type 1 diabetes and 72% of young adults with type 2 diabetes have one or more diabetes-related chronic complication or comorbidity, including hypertension, kidney disease, and neuropathy [3].

Diabetes management in adolescence and young adulthood is complicated by a number of developmental considerations, and diabetes adds complexity when navigating standard transitions associated with education, living situation, interpersonal relationships, and employment. For exam-

ple, diabetes management responsibility typically shifts from family-based management in early adolescence to individual management in young adulthood. Young adults diagnosed with diabetes early in childhood may not receive updated or developmentally appropriate education about changing diabetes management needs that arise with age. Peers and romantic partners may have increasing influence on daily diabetes care and related support. Young adults often struggle to fit diabetes into the erratic schedules and routines associated with college or early employment and experience significant challenges engaging in healthy eating and consistent physical activity. Further, many young adults move out of their family's home and work toward financial independence yet must maintain continuous health insurance coverage and have the financial resources to pay for diabetes supplies and other costs associated with managing a chronic disease [4]. These disruptive transitions in social support, environment, employment, and finances occur in parallel with the transition from pediatric to adult-focused healthcare systems.

Adolescents and young adults with type 2 diabetes may experience unique sociodemographic stressors, which create additional challenges in managing their illness. Type 2 diabetes disproportionately affects young people from underrepresented racial/ethnic minority backgrounds (particularly Native American, non-Hispanic Black, and Hispanic youth), as well as young people with low socioeconomic status. These sociodemographic circumstances contribute to high levels of chronic stress. Indeed, two-thirds of adolescents with type 2 diabetes have been exposed to at least one stressful life event, and increased exposure to stress contributes to deteriorations in medication adherence and quality of life [5]. Further, nearly 90% of young people with type 2 diabetes have a positive family history of diabetes, and witnessing the negative health consequences of diabetes among loved ones can contribute to hopelessness [6, 7].

Diabetes management is complicated by general and diabetes-specific psychiatric comorbidities during this developmental period. Adolescence and young adulthood is a peak time for the onset of mental health disorders, with the major-

ity of mental health disorders presenting prior to age 24 [8]. Representative studies suggest up to 40% of adolescents and young adults with youth-onset diabetes report elevated depressive symptoms [9, 10], and adolescents with type 2 diabetes endorse higher levels of depressive symptoms than those with type 1 diabetes [11]. It can be difficult to separate depressive symptoms from diabetes-related distress or negative emotions arising from the demands of daily diabetes management, particularly as a similar percentage of adolescents and young adults report impairing diabetes distress [12]. However, both depressive symptoms and diabetes distress are associated with poorer diabetes self-management, including less frequent blood glucose monitoring and higher A1c values, and require attention in this population [12, 13].

Adolescence and young adulthood is also a period of increased engagement in risky behaviors. While youth with diabetes do not necessarily engage in higher rates of risky behaviors than youth without chronic conditions [14], there are specific implications for risky behaviors on diabetes management during the transition to adult medical care. Disordered eating is common among transition-aged youth with diabetes. Up to one-third of women with type 1 diabetes report disordered eating behaviors [15]. In addition, over a quarter of young people with type 2 diabetes report clinical or subclinical levels of binge eating disorder, which contributes to increased depressive symptoms and decreased quality of life [16]. Young adults with type 1 diabetes report similar rates of substance use as the general population, and alcohol, tobacco, and drug use can place youth with diabetes at higher risk for acute and chronic diabetes-related complications [17]. These developmental and psychosocial concerns pose specific challenges for transition, particularly as adolescents and young adults are entering an adult care setting, which may not have access to targeted behavioral or mental health resources for youth with diabetes. In fact, a recent survey of US adult endocrinologists identified significant barriers to diabetes management for young adults with depression, substance abuse, or disordered eating in the adult care setting [18].

Treatment and Screening Recommendations

Treatment of youth-onset diabetes during adolescence and young adulthood is focused on minimizing the risk of acute and chronic complications while also supporting increasing youth knowledge of and responsibility for daily diabetes care. Given physiologic, developmental, and healthcare system challenges, providers must frequently monitor and adapt treatment to meet each patient's individual needs. It is recommended that transition-aged patients with diabetes have quarterly appointments with an endocrinologist or diabetes specialty care provider and that each visit include measurement of A1c level, body mass index (BMI), and blood pressure along with review of downloaded glucose data. Routine assessments for all transition-aged youth with diabetes include a lipid panel and urine microalbumin-to-creatinine ratio, as well as routine dental care and evaluation by an ophthalmologist every 1–2 years. For youth with type 1 diabetes, thyroid-stimulating hormone (TSH) and a celiac panel (tissue transglutaminase IgA with normal total IgA or tissue transglutaminase IgG and deamidated gliadin antibodies) are also recommended, while youth with type 2 diabetes should have routine evaluation for nonalcoholic fatty liver disease (NAFLD) [19, 20]. Reproductive health is of paramount importance during this age range, and sexual and reproductive health, family planning, and preventive measures should be routinely discussed as a part of diabetes care. Finally, discussion of high-risk and lifestyle activities (e.g., smoking, drinking, and drug use) also needs to occur routinely during adolescence and young adulthood. Yet data indicate that pediatric providers do not regularly assess for knowledge of and engagement in risky behaviors that may affect diabetes management, such as sexual activity, alcohol use, and pregnancy planning [21]. These topics should be regularly queried and addressed in youth with diabetes without caregivers present.

Routine screening for psychosocial concerns can aid in the treatment of transition-aged youth. The use of formal screening measures ensures routine, consistent assessment of key

behaviors and thoughts. It is recommended that adolescents and young adults complete at least annual assessments on behaviors commonly seen during this developmental period, including depressive symptoms, diabetes-related distress, eating behaviors, and substance use, provided that there are resources in place to meet the needs of patients who report psychosocial concerns [22].

Effective treatment and screening in transition-aged youth with diabetes require developmentally specialized care. The simplest first step is to start seeing patients alone for diabetes care starting around age 12 or soon after diagnosis for youth diagnosed in adolescence. Starting early in adolescence is important to encourage the development of shared decision-making, normalize discussions of sexual activity and risky behaviors, and prompt teens to ask questions and disclose information that may not be shared if caregivers are present. Incorporating these developmentally specific practices in routine diabetes care leads to a more organic, integrated focus on the transition process rather than perceiving transition planning as something extra in the medical visit.

Healthcare Process

The majority of youth with diabetes transfer from a pediatric diabetes care provider to an adult diabetes care provider between ages 18 and 22, with a median age of 19.5–20 years in the US [23, 24]. Engagement in specialty endocrinology care in young adulthood is particularly important for youth with type 1 diabetes, as seeing a general practitioner rather than an endocrinologist has been associated with less frequent diabetes-focused visits [25]. Research and clinical recommendations regarding appropriate care providers for young adults with type 2 diabetes are lacking. However, given that youth-onset type 2 diabetes has been shown to progress quickly, with a poorer response to treatment and higher rates of complications and mortality compared to type 1 diabetes or older-onset type 2 diabetes, specialty endocrinology care is likely the most appropriate setting for treatment [3, 6].

Because the pediatric and adult diabetes healthcare systems typically have vastly different structures and expectations, it is critical to prepare patients for these anticipated changes. For example, pediatric endocrinologists generally work as part of a multidisciplinary, comprehensive team. Appointments are longer in duration and include perspectives of youth and caregivers, allowing for greater coordination of care between the family and provider. In comparison, adult endocrinologists primarily care for an older adult patient population with type 2 diabetes, whose care needs differ substantially from young adults with either type 1 diabetes or youth-onset type 2 diabetes. Additionally, routine diabetes care visits in an adult clinic are shorter and often do not include multiple informants other than the patient.

Adolescents and young adults with diabetes have identified numerous barriers to an optimal transition process. Approximately 25% or more of young adults with type 1 diabetes report a significant gap in medical care (>6 months) during the transition to adult medical care [25, 26]; a survey of 258 young adults with type 1 diabetes who had transferred to adult diabetes care found young adults who identified at least one significant transition-related barrier were at a four-fold higher risk for a gap in diabetes care [27]. Patients are not always prepared for the adult healthcare system and may not receive resources or education about what to expect. Young adults have also expressed challenges with maintaining adequate insurance coverage and paying for diabetes care and supplies [28]. Other barriers related to transition include anxiety and sadness about leaving their pediatric care team, difficulties of finding an adult endocrinologist, long wait times for appointments, difficulty accessing diabetes-specific technology, and poor care coordination [29, 30].

Pediatric and adult endocrinologists also identify challenges with the transition process for patients with diabetes. Pediatric providers commonly report emotional and logistical barriers to transition, including difficulty letting go of pediatric patients and connecting patients with adult endocrinologists knowledgeable of developmental needs and treatment considerations specific to type 1 diabetes and youth-onset type 2

diabetes [31]. Adult providers report inadequate patient preparation in pediatric care, lack of mental health support in adult care, and difficulties obtaining medical records from pediatric care. Both adult and pediatric providers report inadequate training related to the transition process, which has the potential to negatively impact patient health outcomes and engagement in continuous medical care [18].

Condition-Specific Transition Guidelines

Expert-driven guidelines for diabetes transition have been developed by leading national and international diabetes organizations. Although these guidelines primarily draw upon research and expert opinion pertaining to type 1 diabetes, issues surrounding transition for type 2 diabetes are anticipated to be similar. In 2011, the American Diabetes Association Transitions Working Group released a position statement on the transition from pediatric to adult diabetes care systems [32]. This statement provides an overview of the challenges of diabetes in late adolescence and young adulthood and offers recommendations to improve clinical care [32]. The 2018 International Society of Pediatric and Adolescent Diabetes' (ISPAD) Clinical Practice Consensus Guidelines also address the transition process [33]. Other clinically relevant models for transition care include Got Transition (www.gottransition.org) and the Endocrine Society's Type 1 Diabetes Toolkit (<http://www.endocrinetransitions.org/type-1-diabetes>). Theoretical models of transition also have been applied to diabetes. For example, the social-ecological model of readiness for transition (SMART) identifies key modifiable factors to support the transition process, such as disease knowledge and beliefs, motivation, communication with healthcare providers and caregivers, and maturity [34]. We draw from these guidelines and care models to provide specific recommendations to support best practices in transition from pediatric to adult care for youth with diabetes (see Table 6.1). Select resources for enacting these best practices are also presented (see Table 6.2).

TABLE 6.1 Best practices to support the transition from pediatric to adult diabetes care

Youth with diabetes	Parents and caregivers	Healthcare providers	Healthcare system
Ask for information related to benchmarks for diabetes management and transition if not offered	Ask for information related to benchmarks for diabetes management and transition if not offered	Introduce transition policy to patients and families in early adolescence	Have a transition policy
Assume increasingly independent responsibility for diabetes care in adolescence	Support increasing responsibility for youth diabetes care in adolescence	Support increasing youth responsibility for diabetes care in adolescence	
Identify gaps in knowledge and transition readiness skill deficits	Support youth acquisition of transition readiness skills	Assess and identify key transition readiness skills	Incorporate transition readiness assessment measures into care (e.g., electronic medical record)
Work with caregivers and HCPs to meet goals of transition action plans	Support attainment of goals specified in transition action plans	Jointly create, review, and update transition action plans	Incorporate transition action plans into care (e.g., electronic medical record)

(continued)

TABLE 6.1 (continued)

Youth with diabetes	Parents and caregivers	Healthcare providers	Healthcare system
Participate in clinic visits alone	Allow youth to have time alone with diabetes provider	See adolescents alone for at least part of the diabetes care visit starting at age 12	Allow for youth to be seen alone for part of the diabetes care visit
Openly discuss risky behaviors, mental health, and other factors influencing diabetes	Encourage adolescent discussion of risky behaviors, mental health, and other factors influencing diabetes	Routinely screen for and discuss risk factors that may influence diabetes care (e.g., depression, alcohol use, sexual activity)	Integrate routine screening into diabetes care (e.g., electronic medical record)
Ask questions about transition and adult diabetes care	Assist with logistical tasks associated with the transition process, including accessing and maintaining health insurance	Provide resources and education about the transition process and what to expect in adult diabetes care, including specific adult diabetes care provider referrals	Have written and electronic resources available

TABLE 6.1 (continued)

Youth with diabetes	Parents and caregivers	Healthcare providers	Healthcare system
Know medical history and bring summary of diabetes management to adult care provider		Jointly create summary of diabetes management for patients to take to adult diabetes care	

These best practices are derived from the American Diabetes Association’s Recommendations for Transition to Adult Diabetes Care [32], the ISPAD 2018 Clinical Practice Consensus Guidelines [33], the Endocrine Society’s Type 1 Toolkit (<http://www.endocrine-transitions.org/type-1-diabetes>), and Got Transition (www.gottransition.org)

Transition Policy

It is recommended that each program takes the time to craft a program-specific transition policy. This policy guides patient, family, provider, and healthcare system decisions about the timing and expectations for transition for youth with diabetes. This policy should include information about when an earlier than anticipated transition may be warranted (e.g., pregnancy, change in insurance status) and how the transition process is tailored to each individual patient’s needs. A transition policy may explicitly include key benchmarks in the transition process, including expected skills at key ages/developmental stages, expectations for adolescents to have time alone with their providers, and confidentiality of medical information for young adults.

TABLE 6.2 Select resources related to transition to adult diabetes care

Organization	Website	Target audience	Included materials
College Diabetes Network	https://collegediabetesnetwork.org	Patients, families	Website with resources and related handouts on diabetes management during young adulthood, including managing diabetes at college, employment and diabetes, finding an adult care provider, and addressing diabetes in personal relationships
Endocrine Society Type 1 Toolkit	http://www.endocrinetransitions.org/type-1-diabetes	Healthcare providers, healthcare system	Toolkit with PDF forms ready for implementation in pediatric and adult diabetes care practices. Includes a transition readiness assessment, patient fact sheet, clinical transition summary, and practice-related documents
Got Transition	www.gottransition.org	Patients, families, healthcare providers, healthcare system	A comprehensive suite of resources and related handouts on transition from pediatric to adult medical care. Presents the six core elements of healthcare transition and strategies for implementation. Not specific to diabetes

This table was based, in part, on a table published in Monaghan and Baumann [41]

General guidelines recommend the transition policy is first shared early in adolescence with patients, caregivers, and family members to ensure there is enough time to initiate and undergo the transition preparation process. Caregivers and families play an important role in transition, and it is equally important to inform caregivers about their roles and responsibilities to support transition, including allowing teens to meet with providers alone, supporting increasing patient autonomy for diabetes care, and modeling diabetes-related problem solving as needed. Providers should explicitly discuss a caregiver's shifting role from a diabetes care enactor to a supervisor to a consultant by the time the young adult enters the adult diabetes care system.

Transition Assessment and Planning

Broad models of the transition process frame preparing for adult medical care as an iterative process of assessing knowledge, skills, and attitudes related to transition constructs and enacting transition plans to ameliorate identified gaps. Thus, routine assessment of transition-related skills is recommended for patients with diabetes, and there are a number of assessment tools that can be used. Diabetes-specific measures also have emerged, including assessment measures as part of the Endocrine Society's Type 1 Diabetes Toolkit. This toolkit offers patient and provider assessments of skills necessary for transition and associated worries, concerns, and burdens. Examples of specific skills include stating target blood glucose ranges and A1c levels, asking questions in medical visits, knowing how to schedule a medical appointment, and understanding how alcohol impacts blood glucose levels. Yi-Frazier and Corathers developed and validated a diabetes-specific measure of transition readiness skills. The Transition Readiness Assessment for Emerging Adults with Diabetes Diagnosed in Youth, or READDY, assesses key knowledge or skill items that are important for overall health and diabetes management during adolescence and young adulthood [35].

Transition plans are specific plans that are enacted to support the patient's acquisition of skills in the transition process. These plans are often linked with knowledge gaps or barriers identified during the assessment of transition readiness skills. It is recommended that these plans are regularly reviewed with the patient, caregivers and family members (as applicable), and healthcare provider. Transition plans should include not only the specific target skill or barrier but also the recommended intervention or plan to improve this area and the outcome or goal indicating that this area is sufficiently addressed. These can be formal or informal, but transition plans work best when there is a clear structure in place for frequent review and modification. Some practices have successfully integrated diabetes transition plans into the electronic medical record, and this practice can lead to greater consistency with patient-provider review and updating. The targeted skills and goals detailed in a transition plan will change as a patient achieves a skill or meets one target and then sets a new target or goal. Targets are also guided by developmental level or age. For example, it may not be a high priority for a 16 year old to know how to contact his or her insurance company, but this would be an appropriate goal for a 19 year old.

Transfer of Care

The iterative process of transition assessment and evaluation leads to the actual transfer of diabetes care from a pediatric provider to an adult care provider. The year leading up to the transfer of care should involve more frequent discussions of the transition process and recommendations for adult diabetes care providers. In fact, young adults name the specific recommendation of an adult diabetes care provider as the most helpful component of the pediatric transition process [36]. Explicit transition resources related to what to expect in adult care, how to navigate the transition to adulthood and adult care, and logistical questions like how to access medical records are also helpful, yet less than 20% of youth with type 1 diabetes report receiving written materials in pediatric diabetes care [21].

It can be beneficial to schedule a specific visit focused on transition in the 6 months prior to the anticipated transfer date to review all of the necessary information and answer questions. Pediatric providers can assist young adults with compiling a clinical summary to share with their adult diabetes provider to facilitate the transfer of care. This clinical summary synthesizes medical data and provides a portable, easily digestible document covering the onset, course, and treatment of the patient's diabetes and any comorbid conditions or complications. This is preferred over requesting medical records, as it may be difficult to obtain a complete summary through the standard documentation from each clinic visit. Templates for clinical summaries are available, including the Clinical Summary for New Healthcare Team template in the Endocrine Society's Type 1 Diabetes Toolkit (<http://www.endocrinetransitions.org/type-1-diabetes/>).

Indicators of a Successful Transition Process

The ultimate goal of the transition process is for the patient to have access to and engage in continuous, developmentally appropriate diabetes care. Benchmarks of a successful transition process have not been established. However, literature suggests key indicators that can be used to evaluate the overall success of the transition process. The main indicator is engagement in adult diabetes care, as indicated by consistent attendance at routine diabetes care visits without significant gaps in diabetes care. Other key outcomes of healthcare transition include in-target glycemic outcomes, maintained or improved diabetes self-management, avoidance of acute complications, high satisfaction with medical care, and overall high quality of life [37].

Special Considerations for Transition in Youth-Onset Diabetes

While we have presented best practices and guidelines for a successful transition, it is important to individualize the transi-

tion process to best meet the particular needs of each patient, availability of care services, and policies and resources of individual programs. It is particularly important to engage youth at risk for poor outcomes post-transfer, including those with lower family income, who live in areas with low physician supply, or who have a history of out-of-target A1c levels in adolescence [38,39]. There are significant consequences associated with gaps in diabetes care, and additional time and support in pediatric diabetes care may decrease the risk of disengagement from adult diabetes care. Similarly, adult diabetes providers should work to engage at-risk patients by accommodating their needs and schedules as possible. Incorporation of developmentally specific, innovative interventions and resources in pediatric and adult care can maintain engagement in diabetes care and contribute to a successful transition.

Key Resources for More Information

There are a number of print and online materials that provide clear, step-by-step guidance to the transition process. The 2011 position statement on diabetes care for emerging adults provides an excellent overview of best practices for the transition process and potential challenges that may require attention across the transition from pediatric to adult diabetes care [32]. Got Transition provides a primary care transition framework that can be adapted for type 1 or type 2 diabetes, and the Endocrine Society's Type 1 Diabetes Toolkit provides comprehensive provider resources for practices to implement with youth with type 1 diabetes. The College Diabetes Network (www.collegediabetesnetwork.org) has booklets and resources freely available for patients and caregivers related to education, employment, finding an adult diabetes care provider, alcohol and diabetes, and other key topics. See Table 6.2 for more information about how to access these key resources.

As part of the efforts to disseminate knowledge about the specific needs of adolescents and young adults with diabetes,

it is essential that providers take advantage of existing resources and training opportunities on transition. Lack of provider knowledge of best practices on transition has been associated with more barriers to the transition process [31]. Practices should highlight transition resources during staff meetings, journal clubs, or professional development workshops on a regular basis.

It can be challenging to implement resources and reorganize a multidisciplinary team around transition to adult diabetes care. It is recommended that each practice identify a champion or leader to direct or support a transition program and the implementation of key steps in the transition process. This champion may be a nurse, social worker, dietitian, physician, psychologist, or specific transition coordinator or navigator hired for this role. If adding additional staff like care navigators is cost-prohibitive to a practice, it does not mean that the transition process will not be successful. Existing teams can optimize current resources to ensure that all members of the team are comfortable with this developmental focus.

Looking across resources and existing literature, there are a number of components of the transition process that enhance the likelihood of success. Successful programs in pediatric and adult care have identified late adolescence and young adulthood as a distinct developmental period and designed clinical services to meet their needs. It is helpful when diabetes care providers possess specific expertise and interest in the late adolescent/young adult developmental period. Medical clinics for transition-aged youth should have resources and materials for adolescents and young adults prominently displayed and should have opportunities for youth to engage with other young adults with diabetes when possible. Further, it is recommended that clinics are sensitive to the needs of this busy and mobile group, offering visits in the evenings or weekends or via telemedicine, providing reminders for attendance, and utilizing technology to engage with patients. Finally, parents, caregivers, and supportive family members continue to play an important role in diabetes management into early adulthood and the

provision of resources and opportunities for developmentally-appropriate involvement of families can enhance overall transition care for youth with diabetes [40].

Conclusion

Late adolescence and young adulthood is a particularly risky period for diabetes management. Although this age group brings specific developmental challenges, it is rewarding to work with transition-aged youth with diabetes as they assume greater responsibility for and engagement in their medical care. We have detailed evidence-based practices and specific resources that can be used to facilitate a successful transition from pediatric to adult diabetes care. Innovative additions such as telemedicine and related technology can enhance current best practices and reduce gaps in diabetes medical care. Overall, these strategies can assist pediatric and adult care practices in the provision of developmentally tailored, seamless care for adolescents and young adults with youth-onset diabetes.

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Chapter 7

Transition Considerations for Turner Syndrome



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139

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Turner syndrome affects approximately 1 in 2000 live-born phenotypic females, which makes the condition one of the most common chromosomal abnormalities [1–3]. Due to the complex and chronic nature of this syndrome, there is an ever increasing need for an integrated approach to the management of healthcare across the lifespan for girls and women with Turner syndrome [3]. Collaboration between primary care providers (pediatricians, family practitioners, internists) and sub-specialty providers is essential to address the multifaceted and time-intensive care issues specific to individuals with Turner syndrome. This chapter provides an overview of considerations for transition between pediatric and adult care for young women with Turner syndrome. Special attention is given to developmental and psychosocial issues, treatment, and screening recommendations related to endocrinology, cardiovascular health, and gynecology, as well as the value of peer support systems, advocacy groups, and social networking.

In the United States, pediatric endocrinologists have often played a primary role in care of girls with Turner syndrome for oversight of growth hormonal therapy and induction of puberty. During adolescence, the frequency of medical visits for girls with Turner syndrome often decreases as the need for intensive interventions with growth hormone and puberty induction are completed. However, women with Turner syndrome continue to have lifelong medical needs. Many young adult women with Turner syndrome experience inconsistent care in the transition between pediatric and adult care, which can result in under-

recognition and treatment of common comorbidities with sub-optimal outcomes [4–6]. Reported rates of inadequate follow-up range from 12% to 30% [5, 7, 8]; however, a French national registry study of young women with Turner Syndrome found that even if an adult care visit occurred, only a small minority, 20 of 568 (3.5%), had undergone all recommended clinical assessments within the last 4 years [4]. Knowledge of personal medical history, understanding of future health risks and impact of self-care behaviors, health navigation, and health literacy skills are all important aspects of transition readiness to assure adolescents and young adults are equipped to advocate if necessary and maintain ongoing engagement with appropriate healthcare services. At all ages, partnership with primary care providers is essential.

Developmental and Psychosocial Issues

Among girls and women with Turner syndrome, the developmental transition to greater independence includes increasing responsibility for chronic medical and mental health needs in the context of a number of major health and well-being issues [1, 3, 9]. Turner syndrome has a well-defined cognitive phenotype characterized by relative verbal strengths and mild to severe difficulties in attention, executive functioning (including speed of processing), visual-spatial abilities, and visual-motor/fine motor skills. Impairment in social cognition is often present. Given the cognitive risks/deficits and potential psychosocial problems, concerns are often raised throughout childhood about adaptive functioning and functional independence but never more so than during the transition to adulthood [1, 3]. Across the lifespan, (childhood, adolescence, adulthood, and mature adulthood), four key challenges emerge for girls and women with Turner syndrome with infertility the most frequently cited, followed by short stature, sexual function, and general health as other three significant concerns [10]. Each of these areas is impacted by the cognitive and social skills of the woman with Turner syndrome.

The discrepancy between verbal and visual skills, coupled with fine motor deficits and weaker social-emotional functioning, is consistent with nonverbal learning disorder [11, 12]. Nonverbal learning disorder involves difficulty processing visual, spatial, and tactile information [13]. The extent of manifestation of the cognitive phenotype is influenced by karyotype, with mosaicism (45, X/46, XX karyotype) the least severely affected [14]. This pattern of cognitive deficits can be detected early in childhood and persists well into adulthood [15] varying over the course of development. Hormone-mediated cognitive influences are believed to contribute, at least in part, to the cognitive profile. Specifically, deficient levels of estrogen are thought to play a role in memory, motor speed/reaction time, and recognition of facial expression. This premise is partially supported by evidence of improved cognition with estrogen treatment, specifically in memory and motor skills [16]; however, even with estrogen treatment, cognitive deficits have been shown to persist into adulthood [15]. Neuropsychological evaluation at key school transitions has been advised as standard of care [3].

Although evidence is emerging relating neuroanatomical differences to specific cognitive functions in Turner syndrome [17], the question remains as to how this cognitive profile manifests in day-to-day functioning. Often most critical to younger patients is the impact on academic functioning. Many studies on Turner syndrome have attempted to draw specific parallels between the visual-spatial deficits and math performance. Girls with Turner syndrome showed greater difficulty on object perception (“what”) and spatial memory (“where”) tasks and had lower math performance than girls with fragile X or normative controls [18, 19], and the math deficits also persist over time [20]. Women with Turner syndrome have been found to show deficits in quantity processing (cognitive estimation, rapid quantification) and all calculation tasks except multiplication (i.e., addition, subtraction, and division) [21]. In contrast, reading is often a relative academic strength [22].

Following graduation, some degree of proficiency in math is required for most jobs as well as many household tasks. Aside from basic understanding of money and time, adult-

hood demands appreciation of such routine tasks as: pay and benefits (insurance, retirement, investment), deadlines, budgeting and bill management, financing a car or home, medical care appointments and costs, and taxes; daily tasks like cooking or laundry also involve other math skills, such as capacity/volume and temperature. Also vital to academic functioning, and later to vocational success, is attention and executive functioning. Executive skills are higher-level cortical processes that are recruited to organize, direct, and manage everyday demands for purposes of problem solving. For girls and women with Turner syndrome, deficits have been found spanning virtually all facets of executive functioning, including working memory, processing speed/efficiency, mental flexibility, planning, organization (though largely tied to visual-spatial information), and inhibitory control [23].

Additionally, girls with Turner syndrome have much higher prevalence rates of attention-deficit/hyperactivity disorder (ADHD) than girls in the general population [24], sometimes as high as an 18-fold increase [25]. Longitudinal outcomes for girls with Turner syndrome and ADHD are limited. However, the risk of widespread and persistent cognitive, behavioral, and academic impairment is well-established in the general ADHD literature. Adults with ADHD and executive dysfunction have significant functional morbidity affecting school functioning, social class, and educational and occupational attainment in addition to social and leisure functioning beyond the diagnosis of ADHD alone [26].

The focus on academic and vocational functioning, though important, is only one consideration of functional implication of the Turner syndrome cognitive phenotype that also includes broader psychosocial functioning [27]. Historically, women with Turner syndrome have been viewed to have good overall psychosocial functioning, with prevalence rates of psychiatric diagnoses similar to general adult rates [28]. However, psychosocial challenges are commonly reported by girls and women with Turner syndrome and their families, with impairment in social cognition often viewed as a key component. Women with Turner syndrome have been found to have prob-

lems recognizing complex emotions, especially in pairing complex emotional expressions with the corresponding emotional label [29, 30]. Women with Turner syndrome report significantly higher social anxiety, shyness, and depression and lower self-esteem compared to controls [31]. Women with Turner syndrome also find it more difficult to make friends and enter into sexual relationships [32], becoming sexually active at a later age than peers [33]. Limited or absent sexual experience has been associated with low self-esteem and low social adjustment for this population [34]. However, there is some suggestion that starting estrogen replacement therapy in early adolescence may enhance self-esteem and psychological well-being in adulthood [35].

Families also express concern about their ability to achieve adult milestones. Driving is frequently a concern voiced by parents, given deficits in visual-spatial abilities, attention, and executive functioning. To date, there are no known studies examining driving ability in Turner syndrome. However, literature on populations with ADHD [36] suggests that women with Turner syndrome and comorbid ADHD are predicted to be at high risk of poor driving performance. Parents of girls with Turner syndrome rate their daughters as less socially competent than peers [24], and women with Turner syndrome are more likely to live with their parents into adulthood than are peers [37]. However, a significant number of women with Turner syndrome also go on to complete a university degree. Postsecondary education has been increasingly possible for students with learning and/or cognitive difficulties. Students with disabilities who graduate college display similar employment rates and annual salaries compared to students without documented disabilities.

Peer Support, Advocacy Groups, and Social Networking

Involvement in support group events outside the medical clinic is encouraged for women with Turner syndrome. Depending on the availability of a support group in the local

area, there are opportunities to connect with other women with Turner syndrome virtually through social media platforms. Interacting with other women with similar health concerns provides an avenue for peer support. Among individuals with chronic conditions, family and peer support can lead to improvement in behavioral and emotional well-being [38]. For individuals with Turner syndrome, peer support can be a valuable adjunct to the medical care they receive to provide opportunities for fostering social interactions, shared experiences, and resources with respect to education or employment. Turner syndrome advocacy groups have taken a lead in providing educational and networking forums for patients, families, children, adolescents, and adults with Turner syndrome. These advocacy efforts continue to lead important advances in research and improve the care for girls and women with Turner syndrome. Engagement between clinicians and Turner syndrome advocacy groups is especially important during the period of transition between pediatric and adult care to promote engagement and continuity for adolescents and young adult women with Turner syndrome.

Treatment and Screening Recommendations

Endocrinology Considerations

Transition is an important opportunity to provide anticipatory guidance about ongoing screening and prevention guidelines for adult women with Turner syndrome. Prior to transfer, patients should be advised that adult endocrine care for women with Turner syndrome may follow a more consultative model than pediatric endocrine care, with annual visits to maintain a comprehensive approach to screening and prevention services for common comorbidities [3]. The goal of the annual assessment is to monitor blood pressure, oversee ordering and interpretation of appropriate labs and tests (e.g., DXA, EKG, audiology) and referral services, and provide select treatments and interventions (Table 7.1). Visit content

TABLE 7.1 Screening recommendations for adolescents and young adults with Turner syndrome

Provider/service	Screening recommendations	Frequency in adult care
Primary care physician or adult endocrinologist	Weight/BMI Blood pressure	At least annually
	Laboratory studies: thyroid function, liver function, lipids, hemoglobinA1c	Annually
	Laboratory studies: celiac screening, vitamin D levels	Every 2–3 years
	Bone mineral density (DXA)	Every 5 years
Gynecology	Physical exam with cervical cytology	Annual evaluation initiated by age 21; cervical cytology every 3 years
	Screening for sexually transmitted infections including HIV	As indicated for sexually active women based on risk factors, exposures, and geographic region
	Counseling on contraception, family building desires, and fertility options	As needed
Cardiology	Physical exam with electrocardiogram (EKG), 2D-echo or cardiac MRI	Every 1–5 years based upon risk profile
Audiology	Hearing evaluation	Every 3–5 years
Psychology/ neuropsychology	Evaluation and/or counseling	As needed

Adapted from Gravholt et al. [3]

should also cover lifestyle factors such as exercise, diet, and weight control with prevention and screening for metabolic health concerns [3]. Psychosocial issues, including academic and professional life, relationships, sexual function, and plans for future fertility or family building are also relevant. Adult endocrinologists or primary care providers with experience in Turner syndrome can help identify appropriate adult specialists required for comprehensive care. The adult endocrinologist may prescribe estrogen replacement and manage hypertension and hyperlipidemia or may coordinate this care with primary care, gynecology, or cardiology, respectively. Frequency of visits for adult endocrinology care will depend upon required interventions but are recommended at least annually to avoid loss to follow-up and ensure comprehensive and coordinated care.

Cardiology Considerations

Potentially life-threatening consequences of TS are related to the cardiovascular effects, which are associated with increased mortality and morbidity [1]. Therefore, transition is a crucial time to inform young adults of the need for lifelong cardiovascular health surveillance. One of the most common features is systemic hypertension, affecting up to 25% of girls and 50% of adult women with Turner syndrome [39], and approximately 50% of girls have congenital heart defects or aortic disease [40–42]. Women with Turner syndrome are at increased risk for hypertension, obesity, hyperlipidemia, diabetes, stroke, and ischemic heart disease [43] and should be encouraged to maintain a healthy weight and exercise regularly. Adult screening recommendations are summarized in Table 7.1.

One of the most serious concerns in patients with Turner syndrome is the risk of aortic dilation and dissection. Aortic dilation has been reported in up to 6% of patients with Turner syndrome [39], and although rare (1–2%) [40], dissection is often fatal [44]. Congenital heart disease and hypertension are thought to increase the risk of dilatation and

dissection. Commonly encountered cardiovascular and aortic anomalies that can increase risk include bicuspid aortic valve [16%], coarctation of the aorta [11%], elongation of the transverse arch [50%], partial anomalous pulmonary venous return [13%], and persistent left superior vena cava [13%] [1, 40]. The aortic size index (the absolute aortic diameter in cm divided by the body surface area) is used to predict risk for aortic dissection in Turner syndrome rather than absolute measurements to account for short stature [45]. Dissection most commonly occurs in women with Turner syndrome who are an average of 35 years old but ranges from 18 to 61 years old [46]. However, dissection has been documented in patients without known risk factors. Therefore, as part of transition and routine adult care, patients should be counseled to monitor for chest, neck, shoulder, back, or flank pain, particularly if it is sudden and severe, and to seek immediate evaluation [3].

Prior to transition, an electrocardiogram and transthoracic echocardiogram are recommended to screen for cardiovascular anomalies and aortic disease [3]. Cardiac MRI is an effective tool for diagnosing elongation of the transverse aorta, aortic coarctation, and partial anomalous pulmonary venous return [42] and therefore is also recommended [3]. The frequency of repeating echocardiograms and cardiac MRIs to monitor for aortic dilation is based on patient age and risk profile. Optimization of medical management and surgical consultation is recommended for those with an increase in indexed aortic size >1 or an absolute increase in aortic diameter >0.5 cm over a 1 year period. Due to the risk of aortic dissection, patients with mild aortic dilation are suggested to limit sports participation to low and moderate static and dynamic competitive sports, and individuals with more significant aortic dilatation are suggested not to participate in any competitive sports [3]. Transition to adult care offers an important opportunity to engage with adult cardiology and determine individual risk and recommended frequency for ongoing surveillance and activity guidance in adulthood. Based on expert consensus opinion [3], medical management

of hypertension with beta blockers and/or angiotensin receptor blockers is suggested based on age and risk stratification. Treatment recommendations for hyperlipidemia do not differ from the general population [3].

Women's Health Considerations

Care of the young adult patient with Turner syndrome requires a gynecologist with knowledge of their unique and complex health needs, including management of ovarian dysfunction and its sequelae in addition to other comorbidities [1, 47]. In addition to specialized care, routine gynecologic needs should be met and young women counseled and offered age- and risk-appropriate health screenings and contraception as indicated. In women who retain ovarian function, a discussion on pregnancy intentions and fertility preservation options if desired should be addressed. In patients who desire pregnancy, referrals to an infertility specialist and high-risk obstetrician for preconception counseling are imperative as pregnancy is associated with increased fetal and maternal morbidity.

Delayed sexual development, lack of sexual arousal, and/or difficulty during intercourse may result in problems with initiating or maintaining sexual relationships and function [10]. However, assumptions regarding sexual practices should not be made, and counseling on age-appropriate preventive gynecologic health screening is recommended for patients with Turner syndrome as for any other group of women [48]. An annual gynecologic visit is recommended and provides an excellent opportunity to counsel patients and minimize health risks. Women with Turner syndrome should be advised on what to expect with their initial gynecology exam. In addition to a general physical examination, some women will have a pelvic and clinical breast examination. The pelvic exam involves inspection of the external genitalia and surrounding structures, speculum examination of the vagina, and cervix and bimanual exam to evaluate the uterus, cervix, and

adnexa [49]. In patients who are hypoestrogenic, a vaginal exam may be associated with significant discomfort. As such pelvic exams should move at a pace that is comfortable for the patient. The woman should be counseled on the indications and reassured as to her control over the exam. Patients who are sexually active should be counseled on the use of contraception to prevent unintended pregnancy. Although rare, spontaneous pregnancy is reported to occur in about 1.8–7.6% of patients with Turner syndrome [50–53]. Recommendations for the safe use of contraceptive methods for women with various medical conditions can be found on the CDC US Medical Eligibility Criteria for Contraceptive Use (US MEC) and the US Selected Practice Recommendations for Contraceptive Use [54]. The presence of cardiovascular, hepatic, and endocrinology diseases should be considered in counseling for contraceptive options.

Fertility Options

Although some women with Turner syndrome retain adequate ovarian reserve into adulthood and achieve spontaneous pregnancies, the majority become infertile usually before completion of puberty [55–57]. Women who retain function into adulthood exhaust their ovarian reserve at a faster rate, leaving them with limited time during which they can become pregnant or have viable options for fertility preservation [57–59]. In these women, counseling on safety and timing of pregnancy should not be delayed and the discussion should also include the use of assisted reproductive technology (ART) and prenatal genetic testing [1, 3]. Issues surrounding fertility is known to be a significant factor contributing to the quality of life among patients with Turner syndrome and is reported as one of the most painful challenges [10]. Advances in ART and fertility preservation techniques may allow affected women to have a higher chance for a biological offspring [55, 60].

Current established and experimental fertility options include oocyte, embryo, or ovarian tissue cryopreservation

(OTC). Both oocyte and embryo cryopreservation are established methods for young women and girls of reproductive age which involve controlled ovarian hyper-stimulation and oocyte retrieval [60]. Oocyte cryopreservation does not require a partner or sperm donor [60, 61]. There are reports of adult and adolescent patients with Turner syndrome who have cryopreserved oocytes; however to date no pregnancies have been reported in this population [3, 56, 61]. It is important to note that even with newer ART techniques, autologous egg retrieval is often unsuccessful due to low number of viable oocytes; and most women require donor oocytes [3, 60–62]. Ovarian tissue cryopreservation (OTC) is an experimental option done under study protocol for young women and postpubertal girls unable or unwilling to undergo ovarian stimulation and is the only fertility preservation option for prepubertal girls [63]. The process involves surgical (typically laparoscopic) removal of a part or an entire ovary which is the cryopreserved [56] and later reimplanted close to the time of desired conception [61, 64]. Although experimental, to date there are around 60 pregnancies documented including recent reports of successful live births for patients in which the OTC was done premenarchal and prepubertally [64, 65]. As ovarian reserve can be lost even during the very first few years of life, OTC might be the only option for this population although success is questioned given the lower number of expected follicles. As with other fertility preservation options, data on the efficiency of this method among patients with Turner syndrome is lacking, and to date no one with Turner syndrome who has had OTC has returned for transplantation [57].

Pregnancy

Spontaneous pregnancy is more likely in women with 45X, 46 XX mosaicism and those who report spontaneous puberty and menses [52, 53, 60, 66]. Pregnancy in patients with Turner syndrome, whether conception is spontaneous or employed

ART, poses unique challenges and is associated with increased fetal and maternal morbidity and mortality [57, 61]. An overall live birth rate of 54% is reported, with higher rates among those using donor oocytes [60]. There is a reported 20% rate of birth defects in children born to women with Turner syndrome and a higher incidence of chromosomal abnormalities, including trisomy 21 [60]. Spontaneous abortion and miscarriage is also higher possibly due to a combination of uterine factor and fetal genetic abnormalities. In addition, common fetal risks include intrauterine growth restriction, low birth weight, and prematurity [57, 61].

The most significant maternal risks are heart failure, aortic dissection, and sudden death [61]. Maternal mortality among women with Turner syndrome is 100–200 times greater than the general population at 1–2% and is higher among patients who employed ART and those with multiple gestations [3, 53]. Consensus and position statements regarding pregnancy in women with Turner syndrome have been developed by professional organizations which give guidance for preconception counseling and recommendations for pregnancy management [3, 61]. Prior to pregnancy it is recommended that a comprehensive cardiovascular evaluation is done [3]. Preconception aortic size index measurement is strongly recommended, and pregnancy is contraindicated in women with a history of aortic dissection or those with an aortic size index greater than 2 cm/m^2 [3, 57]. Although women found to have cardiac pathology should be aggressively counseled on risks, a normal cardiac testing does not rule out the risk of maternal death from aortic dissection or rupture [3]. In addition to pre-existing cardiac anomalies, connective tissue defects may also predispose to aortic root dissection [57]. It is therefore recommended that all women be counseled on the increased cardiovascular risk associated with pregnancy. Pregnancy among women with Turner syndrome is also more likely to be complicated with thyroid or renal dysfunction, diabetes and severe hypertensive disorders and has a higher risk of cesarean section [55, 57, 59].

Alternative Options for Motherhood

The main objective of fertility preservation is improved psychosocial well-being and promotion of patient autonomy, to allow for the best opportunity to have biological children [61]. However, it is important to avoid producing the psychological damage of false hope as the present techniques of fertility preservation are associated with low success rates and have not been established in the Turner syndrome population [61]. Psychological support is imperative in considering any options for fertility preservation in conjunction with medical counseling on maternal risk. It is recommended that all women with Turner syndrome be counseled on alternative options for motherhood [3, 57, 61]. Gestational surrogacy which entails the planned pregnancy of a woman carried on behalf of another woman with either autologous or donated oocytes and adoption remain very viable options for family building [57].

Healthcare Processes

Health navigation challenges for women with Turner syndrome include, but are not limited to, lack of knowledge about associated comorbidities, suboptimal access to appropriate developmental evaluation, inadequate insurance coverage for diagnostic testing and recommended treatments, identification of knowledgeable providers, and coordination between adult specialists. Recent consensus guidelines highlight models of transition between pediatric and adult healthcare that range from an integrated approach within a single institution or health system to a more fragmented set of pediatric and adult health resources [3]. Increasingly, there is recognition of the value of a care coordinator or health navigator that can help maneuver the complexities of the local healthcare system. A clinic coordinator or health navigator is an individual with understanding of the medical and psychosocial needs of girls and women with Turner syndrome and their families, whose role is to improve the interactions with

the clinical team, engage with community resources, and facilitate a patient-centered approach [3].

Condition-Specific Transition Guidelines

Skill development, essential for successful medical transition, includes “cognitive and social skills to communicate and articulate health needs and preferences” [67]. As communication skills and general health literacy among girls and women with Turner syndrome are relatively high, nonverbal learning challenges or other gaps in health knowledge or transition readiness skills may be missed by general assessments. Therefore, there is growing consensus that condition-specific transition readiness assessments that address the medical, psychological, and cognitive needs of a unique population, such as Turner syndrome, are indicated [68]. Individualized assessment of Turner syndrome-specific content of personal health history and ongoing adult health anticipatory guidance are recommended as part of transition planning. Turner syndrome-specific transition readiness materials include a Turner syndrome passport [69] and the Turner syndrome Pediatric to Adult Care Transition Toolkit (<http://www.endocrinetransitions.org/turner-syndrome/>) available through the Endocrine Society website.

Key Resources for More Information

Additional resources for more information include patient advocacy websites (Table 7.2). Lastly, a parent of a young adult woman with Turner syndrome (written communication with Catherine McCormick, October 3, 2017) offers the following personal insights for successful transition:

A village (team of helpers in the medical, educational, and community arenas) is needed. Transition from child to adult can involve so many aspects of life that many mentors and advisors can benefit the young woman; high school to college or vocational education, getting a job, becoming more self-sufficient and inde-

TABLE 7.2 Key resources for Turner syndrome organizations that provide information and support

Turner Syndrome Society of the United States	http://www.turnersyndrome.org
Turner Syndrome Global Alliance (US)	http://tsgalliance.org
Turner Syndrome Foundation (US)	https://www.turnersyndrome.foundation.org
Turner Syndrome Society of Canada	http://www.turnersyndrome.ca
Asociación Síndrome de Turner México	http://turnermexico.org.mx
Turner Syndrome Support Society (UK)	http://tss.org.uk
Turner Syndrome Association of Australia	https://www.turnersyndrome.org.au
Turner Syndrome International Group	https://tsint.org

pendent, managing finances, redefining yourself to people who have not known you before, self-protection, sexuality, etc...

Clear, repeated, and positive communication among medical providers and my daughter and me helped with the transition. In the medical area, I let her take gradual and incremental responsibility for her own self-care while providing gentle support to allow her to learn to navigate the world of medical appointments, prescriptions, insurance, and billing.

Obtaining assistance from those outside the medical area required that my daughter self-identify as having Turner syndrome and the accompanying learning challenges. People being patient with my daughter helped. In the social world, I offered to have “debriefing” conversations on the finer points of communication, helping to decode the mysteries of human behavior that nonverbal learning disorder misses. Of course, not everyone was patient and understanding, but keeping those instances to a minimum (and avoiding being overwhelmed) helped her focus on problem solving in those fewer difficult situations.

I also knew I could not and should not do everything for her myself. Letting go was important for both of us.

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Chapter 8

Transition Considerations for Congenital Adrenal Hyperplasia



Bonnie McCann-Crosby

Introduction

Congenital Adrenal Hyperplasia (CAH) is a group of autosomal recessive disorders characterized by defects in adrenal steroidogenesis. The most common cause of CAH is due to a mutation in the CYP21A2 gene, leading to deficiency of the 21-hydroxylase enzyme [1]. 21-hydroxylase deficiency accounts for approximately 95% of cases of CAH [2], with less common causes due to other adrenal enzyme deficiencies such as 11 hydroxylase or 3 beta-hydroxysteroid dehydrogenase deficiency [3]. CAH has a wide spectrum of clinical severity depending on the degree of enzyme function. The three forms of CAH ranging from most to least severe include classic salt wasting, simple virilizing, and nonclassical. In those with classic CAH due to 21-hydroxylase deficiency, limited enzyme functionality causes severe defects in both cortisol and aldosterone deficiency leading to a salt-wasting

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161

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condition. Infants can present with life-threatening adrenal crisis in the first few weeks of life, which can include lethargy, poor feeding, vomiting, and electrolyte abnormalities such as hyponatremia, hyperkalemia, and hypoglycemia. Affected females with classic CAH can have virilization of the external genitalia due to the accumulation of cortisol precursors that are diverted to adrenal androgen production. Those with simple virilizing CAH do not have cortisol or aldosterone deficiency, but affected females can present with virilization and both sexes may present with rapid skeletal maturation. Patients with nonclassical CAH typically present later in childhood due to signs of androgen excess such as premature pubarche, accelerated linear growth, hirsutism, or menstrual irregularity [4, 5].

The treatment for patients with classic CAH includes both replacement of cortisol and mineralocorticoid. This complex condition requires lifelong treatment and close monitoring to prevent long-term complications. In childhood, many issues such as growth and pubertal development can be affected, and as patients transition to adulthood, issues such as fertility must be addressed. This chapter aims to explore the various management issues specific to classic CAH in the adolescent period, as well as how to navigate the transition of patients with CAH from pediatric to adult care.

Developmental and Psychosocial Issues

Prior to the adolescent period, education and psychosocial evaluation rely heavily on the parents or caretakers. A shift to focus on extensive education for the adolescent patient and assessment of their knowledge of CAH is needed to prepare them for adulthood. Education at each clinic visit beginning in the early adolescent period should stress the importance of adherence to all medications, instructions on illness management and stress-dose steroids, and long-term endocrine follow-up. Given the complexity of the health behaviors required for successful CAH self-management, receiving education on

multiple occasions over the adolescent years can improve understanding and implementation of the recommendations. The way the information is delivered and taught to adolescents should take into account their emotional state, health literacy, and learning style. Delivering information in different ways, verbally and written, can help meet the needs of patients who have different learning styles.

Psychological support from providers who are experienced in CAH is needed for all adolescents to address issues including quality of life, gender role, sexual functioning, and issues related to having a chronic medical condition. Studies have shown that prenatal androgen exposure in females with CAH has a masculinizing effect, leading to increased aggressive behavior and activity level in childhood [6]. Girls with CAH have been shown to have more masculine playmate selections and prefer a boy-typical play style characterized by more rough and tumble play [7]. Despite more masculine behavior, most females with CAH who are given a female sex assignment after birth typically have a female gender identity, gender role, and heterosexual orientation [8]. Families should be aware, however, that it is not possible to predict future gender identity and sexual orientation and gender shifts are possible. Psychological adjustment in childhood has not been found to be compromised in virilized females with CAH who have been assigned a female sex assignment and treated early in life [9]; however ongoing assessment of satisfaction with gender role and gender identity is needed. Females with CAH have been shown to have delayed sexual milestones such as dating and having intercourse [10, 11]. This may be due to many factors such as concern about genital appearance and body image issues, lack of interest in sex, and decreased clitoral sensation or vaginal stenosis from previous genital reconstructive surgeries leading to discomfort during intercourse. There is a lack of guidelines in terms of how to manage psychosexual issues in patients with CAH; however a multidisciplinary team approach to address issues of gender identity and dysphoria is recommended.

Limited studies have looked at quality of life issues in patients with CAH. A large Swedish study showed that the risk of not completing primary education was higher in females with classic CAH but was not increased in boys [12]. This risk was postulated to be due to the effects of high dosing of hydrocortisone used to suppress androgens in females, leading to cognitive and learning disabilities. In adulthood, additional findings showed that individuals with CAH were more likely to go on sick leave and receive disability compared to controls. Women with classic CAH were less likely to be married compared to controls, and both men and women with CAH were less likely to have biological children than controls. A Dutch study showed that all the adolescents included were satisfied with their own health and overall functioning and they did not endorse problems with concentration, physical discomfort, or pain [13].

Addressing issues such as body image concerns, satisfaction with previous genital surgery, attitudes toward sexual relationships, school performance, and general health are thus an important component to every visit with adolescent and young adult patients with CAH.

Treatment and Screening Recommendations

In childhood, the goals of treatment for classic CAH are to minimize excessive adrenal androgen production by adequate glucocorticoid replacement to prevent virilization and preserve height potential. In the adolescent period, treatment focuses on preventing long-term complications and preserving fertility and sexual function. Both under- and overtreatment with glucocorticoids can lead to long-term complications which can develop in the adolescent period. Inadequate glucocorticoid replacement can lead to early puberty, short stature, virilization, infertility, polycystic ovary syndrome, or testicular rest tumors in males. On the other hand, excess glucocorticoid can also suppress growth due to the effect of excess glucocorticoids on the growth plate

and lead to additional complications including obesity, hypertension, decreased bone mineral density, and potential adverse psychological effects [14]. Excessive mineralocorticoid replacement can cause hypertension, whereas under-treatment can lead to fatigue, low blood pressure, and salt wasting.

Adolescence presents several unique challenges in terms of CAH management. During this time period, pubertal hormonal changes can lead to inadequate suppression of androgens, making control difficult. This is due in part to increased cortisol clearance caused by increases in growth hormone, leading to decreased effectiveness of glucocorticoids [15]. In addition, insulin resistance and increased androgen production during puberty also contribute to management challenges. Issues with treatment adherence often become a concern during adolescence, and for this reason, changing to a long-acting glucocorticoid such as dexamethasone or prednisone is an option after linear growth is complete. Therapy should be individualized and the lowest most effective dose of glucocorticoid is recommended to prevent adverse side effects. Different regimens can include continuation of hydrocortisone, typically ranging from 5 to 10 mg three times daily, longer-acting glucocorticoids such as prednisone or prednisolone (2–4 mg/m²/day divided twice daily), or dexamethasone 0.25–0.375 mg/day [16]. Monitoring for adequate suppression of 17-hydroxyprogesterone and androstenedione is needed to ensure effective treatment. Patients will require increased doses of glucocorticoids in times of illness, trauma, or surgery. For mild illness, the typical recommendation is two to three times the daily maintenance dose of glucocorticoid if patients are able to take oral medications. For patients that are undergoing a surgery or have sustained a major trauma, higher doses of parenteral hydrocortisone are required. Mineralocorticoid replacement therapy typically involves a once daily dose of fludrocortisone ranging from 0.05 to 0.2 mg [16]. Maintaining a plasma renin level on the low end of the normal range and preventing hypertension are the goals for adjusting the mineralocorticoid dose.

Female-specific issues to address in the adolescent period include obesity/insulin resistance, ovulatory dysfunction and menstrual irregularity, and issues related to genital surgery [17]. In addition to using the lowest most effective dose of glucocorticoid, lifestyle management including healthy diet and exercise is important to prevent potential metabolic consequences and maintain a healthy body mass index. Inadequately controlled CAH increases the risk for irregular menses as well as other clinical signs of hyperandrogenism such as hirsutism and increased growth of clitoral tissue. Women with well-controlled CAH are also at risk for irregular menses due to functional ovarian hyperandrogenism and polycystic ovaries [18, 19]. In these patients the addition of oral contraceptives may be useful to restore normal menstrual cycles. Adolescent girls may be more at risk to develop a negative body image if their pubertal development occurs at a different time compared to their peers [20]. Adolescent females who had previous genital surgery may present with several different issues including concerns about cosmetic appearance, urinary incontinence, vaginal stenosis, sexual function, and problems with clitoral sensation. Knowledge of these issues is important for the endocrinologist who is managing these patients, and assessment of potential postsurgical complaints should be part of routine visits. In general, genital examinations should be limited in females unless there are concerns about the adequacy of the vaginal introitus such as pain with the insertion of tampons or sexual intercourse. If a genital exam is needed, it is recommended that it is performed under anesthesia by an experienced surgeon or gynecologist.

Male-specific issues in CAH during adolescence include treatment adherence, risk of testicular adrenal rest tumors, and risk of infertility. Testicular adrenal rest tumors (TART) are often asymptomatic and typically bilateral. Both physical examination and testicular ultrasound are important in evaluating for TART. Progressive TART can cause infertility due to compression of seminiferous tubules which impairs spermatogenesis [21]. Patients with inadequate glucocorticoid

replacement are at increased risk of TART; therefore compliance is critical for prevention. The first-line treatment of TART involves appropriate adrenal androgen suppression with glucocorticoids [22]. Surgery may be necessary when tumors are unresponsive to glucocorticoids, although this usually does not restore fertility [23].

Healthcare Process Issues

Transition from pediatric to adult care is known to be challenging, and unfortunately many patients are lost to follow-up. Beginning early, age-appropriate education about this lifelong condition is essential in the pediatric age group in order to better prepare adolescents for transition. Adolescents must begin to accept responsibility for their medical care and take ownership for administering their own medications as they become more independent. Anecdotal evidence suggests that common barriers to successful transition include lack of knowledge of the patient's disease process, poor disease control prior to transition, and lack of experienced providers in adult care for CAH. Inadequate collaboration and communication between pediatric and adult providers is another challenge to successful transition. Patients may also feel apprehensive about changing to an adult provider who they are not familiar with when they have had a long-term relationship with their pediatric endocrinologist.

Several centers have evaluated the transition process for patients with CAH. A transfer model called the "Kieler Modell" was proposed by Kruse et al. which consists of an outpatient clinic run by both a pediatric and adult endocrinologist [24]. Starting at 17–18 years of age, patients are seen several times by both the pediatric and adult endocrinologists at joint appointments. This process allows improved communication and hand-off between providers, particularly in complex cases with extensive surgical history. Despite having joint visits, long-term attendance has been found to be challenging. A study by Gleeson et al. showed that 50% of ado-

lescents with CAH who were referred to adult providers were lost to follow-up, and introduction of the patient to an adult endocrinologist prior to transition did not have any positive effect [25]. This study did show that patients who attended the first two appointments with adult providers were less likely to be lost to follow-up than those with poor attendance. Another study by Bachelot et al. found that patients with CAH who continued to have regular follow-up after transition to adult care had better physical health, psychological health, and quality of life compared to patients who did not have consistent follow-up [26].

Condition-Specific Transition Guidelines

The transition of the CAH patient from pediatric to adult care should be a planned and organized process that should ideally occur over several years. Figure 8.1 reviews the evaluation and assessment at each developmental stage of CAH in preparation for transfer to adult care (Fig. 8.1). Prior to transition, clinical evaluation should include measurements of height, weight, and blood pressure. Evaluation of menstrual regularity and signs of hyperandrogenism for females and testicular palpation in males should be a part of pre-transition assessment. Biochemical and hormonal parameters should be determined to evaluate the adequacy of medication doses. Transition to a multidisciplinary team that includes an adult endocrinologist, gynecologist/reproductive endocrinologist, and clinical psychologist who has experience with CAH is recommended. Ongoing education of the adolescent patient is needed at each clinic visit in preparation for transition to adult care. Full disclosure of the diagnosis, previous surgeries, and potential physical implications is recommended during the adolescent period, as this can promote a trusting environment between the patient, family, and provider. Patients should be aware of potential long-term complications of CAH and issues related to both over- and undertreatment. Discussions on how to navigate the health-

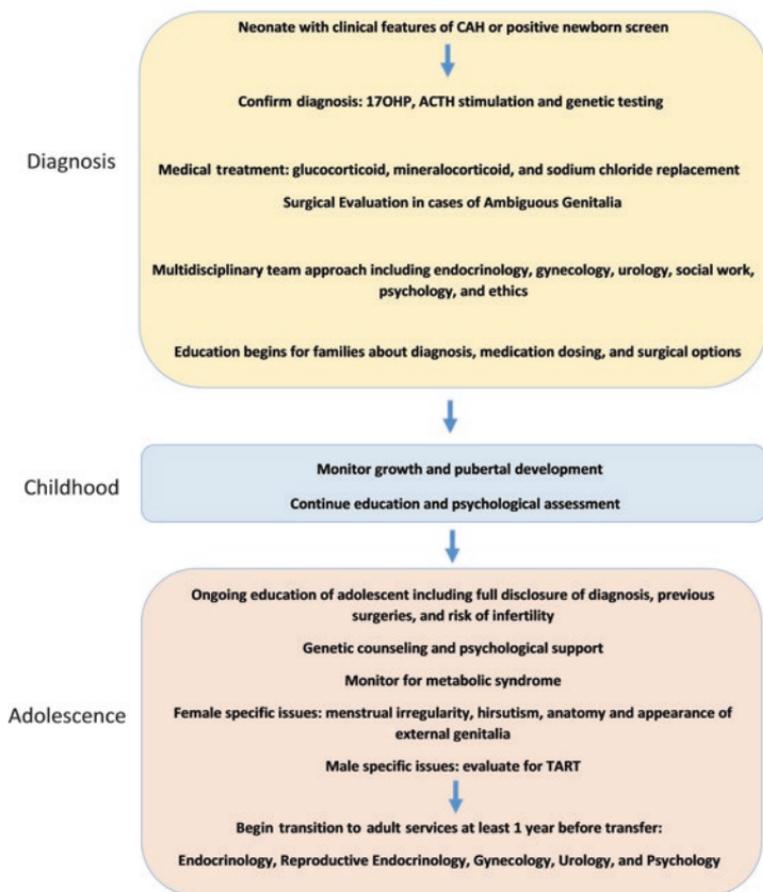


FIGURE 8.1 Approach to the patient with classic CAH throughout developmental stages

care system prior to transition to adult care must be started in adolescence. Genetic counseling is recommended prior to transition to adult care to discuss risks of having an affected child. The patient’s knowledge about CAH should be assessed by their medical providers, particularly regarding their medication regimen, indications for stress dosing during times of illnesses, and surgical history. Psychological support by experienced professionals should be offered to

families and adolescent patients with CAH. Counseling should address issues such as quality of life, treatment adherence, education, sexual orientation, and potential gender reassignment particularly in females with a history of virilization and issues related to previous surgeries and sexual function.

A transition process that is started at least 1 year prior to the anticipated transfer to adult care is recommended and should be individualized to each patient.

Key Resources

Trustworthy web-based resources and parent support groups should also be offered to families at diagnosis. The CARES Foundation (Congenital Adrenal Hyperplasia Research Education and Support) can provide further information and support for patients and families [27]. In addition, families should be provided resources for online professional organizations such as the Endocrine Society and Pediatric Endocrine Society [28, 29].

Conclusions

CAH is a complex condition requiring an experienced multidisciplinary team for optimal management. Ongoing monitoring is essential as these patients are at increased risk for long-term complications both from over- and undertreatment. Educational resources with reliable information such as the CARES Foundation should be offered to families at diagnosis. Psychological support should be offered to all patients and families with this condition. Education and knowledge assessment of families and patients in an age-appropriate manner is necessary to prepare for a successful transition from pediatric to adult care. Starting the transition process early in adolescence may improve regular medical follow-up in adulthood leading to improved quality of life.

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Chapter 9

Transition Considerations for Cancer Survivors with Endocrine Sequela



Vincent Horne and Rona Sonabend

Background

The number of childhood cancer survivors is increasing as remission rates of all childhood cancer types improve. As of 2014, the 5 year survival rate for all cancer types was 84%, with greater than 90% survival rate among childhood leukemia and lymphoma survivors and a 74% rate among childhood brain tumor survivors (which account for 25% and 20% of all childhood cancers, respectively) [1]. This is secondary to advanced techniques in cancer therapy including enhanced radiation technology, drug therapy, and increased access to care in multi-disciplinary centers. Due to improving outcomes, 1 in 750 adults are estimated to be a cancer survivor; an estimated 350,000 childhood cancer survivors are less than 40 years of age, of which nearly 76,000 are young adults aged 20–30 years [1, 2].

As survival has improved, the morbidity and mortality from the late effects of cancer therapy have increased [2, 3]. In fact, the majority of those surviving at age 40 years have a 95% inci-

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175

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dence of at least one chronic health condition and 80% incidence of a serious comorbidity [4]. The pattern of disease burden differs among cancer types and includes endocrine dysfunction or infertility; neurocognitive or psychological abnormalities; gastrointestinal, renal, cardiac or pulmonary sequelae; hearing or vision impairment; neurologic dysfunction; musculoskeletal abnormalities; and secondary malignancies. Endocrine sequelae occur among nearly 45–65% or more of all childhood cancer survivors, with brain tumor survivors at highest risk, typically requiring lifelong treatment and monitoring [3, 4].

As adolescent and young adult cancer survivors become an even larger population, more individuals will require high-quality care long into adulthood, and bridging the vulnerable period of time from childhood to adulthood will become increasingly important.

Endocrine Treatment and Screening Recommendations

Approaches to cancer therapy include surgery, chemotherapy, radiation, and bone marrow transplantation. In determining appropriate evaluation for endocrine sequelae among childhood cancer survivors, endocrine screening should be tailored to the individual based on risk assessment from historical review of the treatment protocols, including the location and type of tumor and relative treatments undertaken. Endocrine late effects may occur around the timing of initial tumor treatment or years following, particularly in the case of radiation therapy [5]. The Children's Oncology Group (COG) has developed screening protocols following cancer treatment that can be referenced to determine individualized screening guidelines based on particular cancer therapies and tumor location [6]. A complete physical exam and targeted biochemical screening are recommended, typically performed annually in long-term survivors (Table 9.1). Treatment should be provided as appropriate based on abnormalities discovered.

TABLE 9.1 Endocrine screening recommendations [6]

Endocrine abnormality	Risk factors	Clinical evaluation	Laboratory evaluation
Growth hormone deficiency	>10–18 Gy to hypothalamus	Growth velocity, height, and weight at each visit	IGF-1, IGF-BP3, growth hormone stimulation testing, bone age Timing: If indicated
Precocious puberty	>18–20 Gy to hypothalamus	Pubertal exam/ growth velocity at each visit	LH, FSH, estradiol, testosterone, bone age, leuprolide stimulation testing Timing: If symptomatic prior to normal timing of puberty (female <8 years, male <9 years)
Hypogonadotropic hypogonadism	>30 Gy to hypothalamus	Pubertal exam/ growth velocity at each visit Symptoms: loss of sexual function (i.e., erections, hair loss, menses, vaginal dryness, low libido)	LH, FSH, estradiol, testosterone, bone age Timing: at 13 years (females) or 14 years (males) as baseline and as clinically indicated

(continued)

TABLE 9.1 (continued)

Endocrine abnormality	Risk factors	Clinical evaluation	Laboratory evaluation
Adrenal insufficiency	>30 Gy to hypothalamus	Symptoms: vomiting, fatigue, weight loss, shock during illness	0800 cortisol, low dose ACTH stimulation testing Timing: at least yearly
Central hypothyroidism	>40 Gy to hypothalamus	Symptoms: fatigue, poor growth, weight gain, cold intolerance, hair loss, dry skin, constipation	TSH, free T4 Timing: at least yearly
Hyperprolactinemia	>40–50 Gy to hypothalamus	Symptoms: galactorrhea, low libido	Prolactin level Timing: if symptomatic
Primary hypothyroidism	>10–20 Gy to cervical neck	Symptoms: fatigue, poor growth, weight gain, cold intolerance, hair loss, dry skin, constipation	TSH, free T4 Timing: at least yearly
Diabetes insipidus	Suprasellar tumor with surgery	Symptoms: polyuria, polydipsia, dehydration	Serum and urine studies (sodium, serum osmolality, urine osmolality), water deprivation testing Timing: as clinically indicated

TABLE 9.1 (continued)

Endocrine abnormality	Risk factors	Clinical evaluation	Laboratory evaluation
Primary hypogonadism	>6 Gy to gonads	Pubertal exam/growth velocity at each visit	LH, FSH, estradiol, testosterone, bone age
	Alkylating chemotherapy	Symptoms: loss of sexual function (i.e., erections, hair loss, menses, vaginal dryness, low libido, infertility, azoospermia)	Timing: at 13 years (females) or 14 years (males) as baseline, and as clinically indicated

Abbreviations: TSH thyroid-stimulating hormone, T4 thyroxine, LH luteinizing hormone, FSH follicle-stimulating hormone, IGF-1 insulin growth factor 1, IGF-BP3 insulin growth factor binding protein 3, Gy Gray

Surgery

Surgical therapy is used for both diagnosis and primary cure, particularly for solid tumors. Newer technologies have improved outcomes by reducing the extent of surgical resection, including subtotal resection or limb-sparing surgeries [7]. Resection or direct injury of organs of hormone secretion may result in endocrine dysfunction following surgery and must be anticipated. Typically, development of hormonal deficiencies follows immediately after surgical intervention. However, for locally aggressive solid tumors involving the pituitary gland such as craniopharyngioma, pituitary dysfunction may be present at the time of diagnosis [8]. Diabetes insipidus is more common among brain tumor survivors who have suprasellar extension, pituitary involvement, or surgical resection of tumors located within the suprasellar region around the hypothalamic-pituitary axis [9]. Hypothalamic obesity may also develop as a result of hypothalamic injury

[10–14]. Other neurocognitive injury or pain effects may impact quality of life as well [7, 15–20].

Chemotherapy

Chemotherapeutic agents are used for a broad array of childhood cancers. The effect depends upon the particular agent, tumor type, cumulative dosage, duration of therapy, and administrative route. Alkylating agents such as cyclophosphamide have been shown to have the highest risk of long-term endocrine-related outcomes [6]. Use of alkylating agents and heavy metals are known to cause gonadal dysfunction including decreased pubertal hormone production and infertility [15, 16]. In men, higher alkylating doses are responsible for Leydig cell dysfunction manifesting as poor testosterone secretion [16]. Even more common is premature azoospermia which can be seen without reduction in testosterone. Prepubertal status at the time of alkylating agent administration is not protective [16, 21]. In women, doses of alkylating therapy may accelerate depletion of oocytes at a young age resulting in premature ovarian failure, manifesting as delayed puberty, early menopause, or infertility [15]. Abdominal or pelvic irradiation will compound this effect even at low doses [15]. Fertility dysfunction has also been associated with bone marrow transplantation following total body irradiation or high-dose alkylating therapy preparations without irradiation. Among adult childhood cancer survivors, infertility is a primary cause of low quality of life and typically warrants fertility counseling and preservation if possible [22].

Chemotherapeutic agents are also known to affect bone mineralization and possibly cause early osteoporosis. Antimetabolites such as methotrexate, corticosteroids such as dexamethasone or prednisone, and alkylating agents such as ifosfamide are the most commonly recognized causes of decreased bone health [23]. Bone disease is compounded by irradiation to bony structures as well [6, 23, 24].

Tyrosine kinase inhibitors, which target particular oncogenic proteins, are newer agents used in pediatric cancer therapy. While less data is available, endocrine effects have been reported, with thyroid dysfunction, growth hormone deficiency, and infertility being the most common sequelae [25].

Radiation Therapy

Radiation therapy, used with or without chemotherapy and surgery, may lead to local or scattered effects on underlying structures. Radiation therapy may reduce growth due to bone growth plate injury, including proportionate short stature following total body irradiation or disproportionate growth of the spine as in craniospinal radiation [26–29]. Other abnormalities can include thyroid dysfunction following neck irradiation [30, 31]; hypothalamic-pituitary dysfunction following brain tumor therapy [5, 9, 32–34]; reduced pancreatic function and visceral adiposity leading to metabolic disease including diabetes mellitus following abdominal irradiation [35, 36]; and compounded risk of hypothalamic obesity at high doses of hypothalamic irradiation in combination with tumoral or surgical associated injury. The relative effect of secondary injury due to irradiation is predicated upon the type of radiation, cumulative dosage, amount of fractionation, duration, age at time of treatment, and location of irradiation target [6, 21].

Children with brain tumors are often subjected to high-dose irradiation between 20 and 50 Gy localized to the tumor and suspected metastatic beds such as the spine, dependent on the tumor diagnosis [37]. Irradiation at these higher doses subject survivors to anterior pituitary dysfunction, dependent on the relative fraction delivered to the hypothalamic-pituitary areas [38, 39]. While growth hormone deficiency is the most common endocrine sequelae among brain tumor survivors due to the relative sensitivity of somatotrophs and

the hypothalamus to radiation, at higher doses of 50 Gy or more, all anterior pituitary deficiencies are likely to develop [21, 39–42]. Hyperprolactinemia may also develop at higher doses of irradiation (>40 Gy) [6, 43]. At intermediate doses of irradiation (~20 Gy or more), precocious puberty may occur. Diabetes insipidus is not seen after irradiation as the relative control of antidiuretic hormone is preserved despite high doses of irradiation (Table 9.1) [9].

Direct neck radiation impacts underlying target tissue, placing those individuals at greater risk for secondary malignancies. In particular, this may include thyroid nodules or carcinoma [44]. Therefore, long-term screening of thyroid cancer is warranted with yearly thyroid exams and subsequent evaluation with ultrasound if nodularity is detected [6]. Low-dose neck irradiation increases the risk for primary hypothyroidism, thus requiring monitoring of thyroid function as well in these individuals [6].

Bone Marrow Transplantation

Hematopoietic stem cell transplantation therapy is associated with endocrine dysfunction due to the preparation treatments which may either include total body irradiation or alkylating chemotherapy [45]. While total body irradiation places survivors at risk of hypopituitarism, obesity, low bone density, primary hypothyroidism, secondary cancers, and metabolic disease, those who receive alkylating therapy for transplant preparation are at higher risk of bone disease and gonadal dysfunction, including both infertility and hypergonadotropic hypogonadism [45–47]. Efforts to understand long-term outcomes of fertility for these survivors are underway, but infertility rates caused by these treatments could be as much as 20–30% or more [45, 47, 48]. Bone marrow transplantation also increases risk for vitamin D deficiency which has been associated with increased mortality in severe cases [49]. Thus, vitamin D replacement therapy may improve bone health and overall outcomes in survivors.

Considerations Among Adolescents and Young Adults

Serial examinations and biochemical screenings to assess endocrine function, provide diagnoses, and begin therapy with hormonal replacement begin immediately following cancer diagnosis. Monitoring of growth and metabolic outcomes also occur regularly. If a child is already receiving hormonal therapy, treatment is usually lifelong and needs continued monitoring into adulthood.

As children transition into young adults, emphasis on adult-oriented sequelae is important. Fertility outcomes are of paramount importance to long-term quality of life in childhood cancer survivors. Infertility may not have been adequately evaluated or discussed with children and younger adolescents, or infertility may not manifest until a later time period. Tissue preservation of the ovaries or sperm, if possible, should occur early in order to preserve long-term fertility, and counseling should be provided about these treatments [21, 22]. Also, early osteoporosis often does not manifest until early adulthood or later. Thus, the evaluation and management of endocrine sequelae needs to extend into adulthood.

Developmental and Psychosocial Issues Among Childhood Cancer Survivors

Childhood cancer survivors are at risk for negative neurocognitive outcomes. Brain tumor survivors report neurocognitive abnormalities as the most common sequelae of their tumor and treatments [3, 50]. Those who receive brain irradiation at younger ages (<4 years) have the highest rates of neurocognitive effects. Effects can include subtle abnormalities such as learning disabilities or development of attention deficit hyperactivity disorder or more severe effects such as developmental delay, blindness due to injury of the optic nerves, memory loss, or motor deficits due to stroke or other injuries

[50]. IQ loss averaging 12–14 points occurs among survivors receiving brain irradiation and can progress even decades later, involving failure to attain age-appropriate attention, working memory, and processing speed [50]. Strategies to reduce these effects have included newer radiation modalities and delaying radiation usage, particularly in those of young age [50]. Measurable improvements in areas of working memory, processing, and potentially global IQ exist for those survivors who have received proton beam versus conventional irradiation [51–53]. However, children receiving only chemotherapy may still develop poor neurocognitive outcomes and difficulty with attention compared to peers, requiring monitoring and evaluation [54, 55].

As primary effects of the tumor and treatments on brain function may have a negative outcome on social interaction, independence, and mental health, reliance on family support is common during the period of transitioning from pediatric to adult-oriented care [2, 56]. Childhood cancer survivors are more likely to live with their parents and have lower rates of marriage, professional/vocational training and employment. They have higher rates of anxiety and depression and suicidal ideation, a major health risk [57–59]. Adolescents and young adults within the first year of diagnosis have a 2.5-fold relative risk of suicidal behavior and a fourfold risk of suicide completion [60].

Neurocognitive and psychological support are therefore important aspects of care throughout the life of a childhood cancer survivor. Childhood survivors require baseline and follow-up neurocognitive and psychological assessments, and intervention is recommended for those identified as high risk [52]. Yearly evaluation of vocational and social progress is likely to help identify those who require neurocognitive intervention [6]. Mental health support should be made available to cancer survivors throughout their lifetime, and recommendations include the use of standardized screening tools for cancer survivors at visits to either specialized care centers or at primary care visits [60, 61].

Transition Issues

Childhood cancer survivors need long-term follow-up care given lifelong risk of recurrent or secondary neoplasms and endocrine, neurocognitive, psychological, and cardiovascular disorders [2, 24, 44]. While many endocrine abnormalities develop in the years immediately following cancer diagnosis, endocrine abnormalities can also present later in adulthood due to continued disruption of hypothalamic-pituitary and other end-organ hormonal functions [56]. Thus, long-term comprehensive care in adulthood includes evaluation and management of bone health, fertility, adult-onset secondary cancer, and pituitary dysfunction among other issues [62].

Ideally, transition of childhood cancer survivors involves a long-term cancer survivorship program which includes adult endocrine specialists. However, barriers may interfere with appropriate transition, including loss of health insurance, neurocognitive and psychosocial limitations, resource inadequacies including limited adult specialist providers, knowledge deficits, and lack of access to prior medical records including previous cancer treatment strategies in childhood [24, 63]. Appropriate planning of information delivery is a key deficiency; while 78% of pediatric institutions are creating or already utilize plan summaries at the time of transition, many primary adult providers report either not receiving these summaries or having inadequate access to prior histories [64]. Therefore, transmission of information including tumor diagnosis, cancer treatments undertaken, and secondary diagnoses is likely to improve care for these adults with complex childhood medical histories. Similarly, planning prior to transition, facilitating access to health insurance, identification of an adult provider including an adult long-term follow-up oncology program or adult endocrinologist, and assessment of knowledge of individual healthcare needs into adulthood are likely to improve the transition period [62, 65].

Healthcare Process Issues

Several institutional and systemic barriers can affect the quality of care that childhood cancer survivors receive into adulthood. Cancer survivors may have limited knowledge of their potential health risks as they enter into adulthood, and healthcare providers may also fail to recognize the unique health risks that adolescents and young adults may have [2]. While survival of their cancer is the immediate focus of attention after diagnosis, cancer survivors later emphasize the late effects of treatment including infertility on limiting their quality of life [3, 22]. Therefore, cancer survivors and their families require ongoing counseling on the risks of treatment and should be offered opportunities to mitigate these risks early in the course of their recovery.

However despite the benefits of continuous care, as the years pass from initial tumor diagnosis, the likelihood of follow-up decreases [2]. Several issues from the patient perspective contribute to reduced visits including lack of understanding of their long-term risks and the wish to move on with their lives. Post-traumatic stress disorder is common and may impact motivation for seeking care [2, 7]. Although involvement in a cancer survivorship program may be the most optimal follow-up, these resources are not available for many adults, with less than 25% of survivors attending a clinic that offers multidisciplinary care. Cancer survivors instead often receive care from primary care providers, who do not have specialized expertise in the endocrine sequelae of childhood cancer or in transition-related issues that are important to this population [2].

Healthcare providers have recognized gaps in knowledge of potential effects of cancer treatment as well. Oncologists and primary care providers may both lack knowledge on appropriate long-term screening based on cancer therapies. Pediatric oncologists may have increasing discomfort in continuing management of childhood cancer survivors into adulthood, but others often prefer to continue long-term follow-up of established patients even into adulthood for

their cancer monitoring due to lack of adult resources [2]. Due to lack of institutional programs for specialized adult survivorship care, primary care providers are often relied upon to deliver care but typically prefer to provide care to cancer survivors with the help of a specialized multidisciplinary center. Institutions may lack financial resources or expertise to run a survivorship program, or programs may limit access based on age as survivors approach adulthood [2]. Once adolescents and young adults move on from their initial medical home, provider and patient knowledge about the types of treatments received and diagnoses may be lost through the transition process to adult providers. Lack of knowledge on the types of therapies previously undertaken increases difficulty in implementing appropriate screening practices. While technological advancements and improvement in institutional information sharing through electronic health records is likely to address these problems, at present interoperability of health record sharing remains limited to only 30% or less of institutions nationally [66].

To improve the knowledge of particular cancer diagnoses, treatments, and appropriate screening recommendations for cancer survivors, large systematic programs including the “Passport for Care” program have been developed so that, regardless of knowledge base, providers and families will have access to all information and subsequently be able to deliver or seek out appropriate care [64]. Passport for Care and similar programs are an online personal repository for patients’ oncological history including treatments and suggest appropriate screening strategies based on individuals’ history and age from diagnosis. Data is stored for future use by patients and providers including adult oncologists, endocrinologists, and primary care providers. Alerts to perform screening based on current guidelines are offered, as dictated by individual histories [64]. This program is designed to improve care delivery regardless of the provider and may improve outcomes by detecting new abnormalities earlier, preventing long-term morbidity and limiting disease burden [2].

Sources for Suggested Reading

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Summary

Childhood cancer survivorship is challenging for transition care into adulthood, in part due to educational, psychosocial, and institutional barriers that providers and cancer survivors are likely to face. Using systematic information databases which allow for sharing of treatment-related risks and screening strategies is likely to improve outcomes for an ever-growing population. While a multidisciplinary care team with access to specialists including endocrinologists knowledgeable in the care of cancer survivors is important, primary care providers are likely to become the primary medical home as young adults transition away from pediatric oncology and endocrinology services. Implementing a shared treatment model whereby the primary care provider, adult oncologist, and specialists work together to provide appropriate screening and treatment may optimally serve the health needs of this vulnerable population.

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Chapter 10

Transition Considerations for Transgender Patients



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A transgender patient transferring from pediatric to adult endocrine care will likely have presented to a pediatric endocrinologist or other healthcare professional as a young child or older youth questioning their gender or asserting a transgender identity (Table 10.1). It is at that point in time that the healthcare professional must start thinking about

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195

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TABLE 10.1 Terminology

Key terms	Definitions
Binary gender	Having a gender identity that is either boy/man or girl/woman
Binding	When a person, typically postpubertal and assigned female at birth, attempts to flatten their breasts to present the appearance of a masculine chest by wearing constricting garments known as binders
Cisgender	Individuals whose gender identity aligns with the sex they were assigned at birth, for example, an adult who was assigned the male sex at birth says that he is a man. In essence, cisgender individuals are those persons who are not transgender
Gender expansive	Anyone whose gender expression differs from what is expected. As language is continuing to develop and shift, terms such as gender nonconforming and gender diverse may also be used
Gender diverse	An umbrella term for transgender and gender-expansive (TGE) individuals
Gender dysphoria (capitalized)	Controversial diagnosis in the DSM-5 (diagnostic and statistical manual of mental disorders 5th ed.)
Gender dysphoria (lowercase)	Discomfort related to one's body not matching their internal sense of gender as well as associated social distress. This is a primary cause of gender stress
Gender expression	Readily visible sets of norms, including behaviors, clothing, hairstyle, mannerism, roles, activities, etc. that are ascribed to one gender or another by a culture. This is typically referred to as masculine, feminine, or androgynous
Gender health	The opportunity for an individual to live in the gender that feels most real and/or comfortable for the individual and the ability for individuals to express gender without experiencing restriction, criticism, or ostracism

TABLE 10.1 (continued)

Key terms	Definitions
Gender identity	One's asserted gender. Their innermost concept of self as boy, girl, both, neither, or another gender (e.g., man, girl, non-binary, agender, or third gender). One's gender identity is how one perceives and knows themselves as well as what they call themselves. Patients should be referred to based on their gender identity; clinicians should ask what name and pronouns patients want to be called and should make sure that they are addressed in this manner consistently throughout the clinic or hospital
Gender marker	The "male"/"M" or "female"/"F" on one's ID, birth certificate, passport, or any other form of legal identification document. Some states are beginning to offer a non-gendered "X" option for the gender marker
Gender transition	An individual process that may consist of social (i.e., shifts in gender expression, name, and/or pronouns), legal (i.e., identification documents), medical (i.e., pubertal suppression, hormone therapy), and/or surgical changes in gender (i.e., facial, chest/breast, genital surgeries)
Honorifics	Forms of address, formal, e.g., Mr./Ms./Mx.
HRT	The acronym HRT is commonly used among transgender people to refer to gender-affirming hormone therapy. This commonly leads to confusion among providers who think of HRT for patients assigned female at birth to be estrogen therapy, when these patients are actually using HRT to refer to testosterone therapy
Misgendering	When an individual is referred to by others with pronouns (or form of address) that do not correctly reflect their gender identity. This experience is associated with increased depressive symptomatology

(continued)

TABLE 10.1 (continued)

Key terms	Definitions
Non-binary gender	A gender identity that is not bound by two options. Any and all genders, never either/or. May identify with identities such as genderqueer, agender, gender fluid, demiboy, etc. Each person's experience of their gender identity is unique and, if asked, many people will be glad to share how they understand and experience their gender identity. Pronouns such as they/them are commonly used by non-binary individuals
Packing	When a person, typically assigned female at birth, attempts to add the appearance of a genital bulge by placing an object (e.g., packer) in their underwear
Padding	When a person, typically assigned male at birth, attempts to add breast forms to present the appearance of breasts
Pronouns	Forms of addressing a person in the third person, e.g., she/her/hers, he/him/his, they/theirs/their
Sex	Includes several components such as one's chromosomes, relative levels of sex hormones post-puberty, internal genitalia, and external genitalia. One's sex is designated at birth – typically male or female – based on the appearance of one component of their sex, their external genitalia
Sexual orientation	Describes one's romantic and/or sexual attractions based on the gender identity of their individual and those of the person or people they are attracted to
Trans feminine	A person who has a feminine spectrum gender identity (e.g., girl or demigirl) but has "male" on their original birth certificate
Trans masculine	A person with a masculine spectrum gender identity (e.g., boy or demiboy) but has a "female" on their original birth certificate
Transgender	Anyone whose gender identity differs from what is expected (typically based on their sex assigned at birth). Includes binary and non-binary gender identities

TABLE 10.1 (continued)

Key terms	Definitions
Transphobia/ transnegativity	A range of attitudes, feelings, and behaviors ranging from the idea that being transgender is less optimal than being cisgender, to hatred and disgust toward anyone perceived to diverge from gender expectations
Tucking	When a person, typically assigned male at birth, attempts to minimize the appearance of a genital bulge by using various methods including gaff panties which create the appearance of a flat front

transition considerations¹ from pediatric to adult care, given critical concerns for the vulnerable population of transgender young adults [1]. The concept of transition from pediatric to adult healthcare for transgender care is quite recent, dating back to the 1990s when clinicians at the VU University Medical Center in Amsterdam introduced the use of GnRH agonists to provide transgender youth with time to further explore their gender identity until the age of majority (age 16 in the Netherlands) while halting the development of their predisposed sex characteristics caused by the onset of puberty [2].

The intervention of pubertal suppression for gender care, along with follow-up consideration for masculinizing or feminizing hormone care, is now used internationally at pediatric gender care programs. Youth under the age of majority are evaluated both by medical and mental health professionals and recommended for one or both gender affirming interventions [3]. Some of these youth are also requesting surgical interventions, such as chest or genital surgeries, to accompany their endocrine gender treatments.

1 *Note.* The word “transition” has another meaning when referring to transgender people. It refers to the individual process transgender individuals go through, a social, legal, medical, and/or surgical processes with the goal of self-actualization as it relates to one’s gender identity and body. The authors will use “gender transition” throughout to refer to this process.

Developmental and Psychosocial Considerations

Before a child ever appears at a pediatric gender clinic for endocrine care, that child will have begun to question or explore their gender. Some of these children will be questioning their *gender identity*, who they perceive themselves as being—a boy, a girl, or something else (e.g., non-binary); some of these children will have been exploring their *gender expressions*—the manner in which they present their gender to the world (i.e., feminine, masculine, some combination of both, or genderless through the clothes they wear, the activities they engage in, the friends they choose, etc.); and some of these children will be exploring both *gender identity* and *gender expressions* [4]. The task for healthcare professionals and family alike is to differentiate between those children who are primarily exploring or delineating their *gender expressions* (i.e., gender expansive) and those children who are declaring a *gender identity* that is discordant from the gender that would match the sex assigned to them at birth (i.e., transgender). It is also possible for young people to be exploring, questioning, or declaring both gender expressions and gender identity (i.e., gender expansive and transgender) simultaneously.

Traditional theories of gender identity have posited a model of development in which a child's gender is fixed and stable by the age of 6 [5–9]. Yet these theories fail to account for the developmental pathways of children who are recognized as gender diverse in gender identity and/or expression. Some transgender individuals question and develop their gender identities well before the age of 6, and some not until later adulthood, leading to the conclusion that gender development is a lifelong process, and it cannot be assumed that one's gender identity is fixed in early childhood [10].

Appreciation of gender identity development as a lifelong process helps endocrine providers follow a shifting terrain of a young person's gender identity or expressions while under their care and emphasizes the need for an interdisciplinary

model of care including both medical and mental health professionals [11]. This interdisciplinary approach is commonly followed in pediatric gender programs as the best standard of care and is equally relevant to adult endocrine care of transgender and gender-expansive patients. Additional care team members may include but are not limited to lawyers, speech therapists, social workers, and spiritual leaders.

Given the complex developmental trajectories of gender identity and relevant to the transition of pediatric to adult endocrine care, three different groups of gender diverse young adults should be identified:

1. *Early childhood presenters*: These patients are young adults who at a very early age indicated that they were not the gender everyone thought they were but rather the other one. When given the opportunity and support, these patients have often already socially transitioned from the gender matching the sex designated at birth to their affirmed gender before seeking adult endocrine care. Many have lived for years in their affirmed gender, some with legal gender marker and name changes, and some already have received puberty blocking treatment followed by hormone therapy. For these individuals, their pediatric endocrine care could be labeled “continuity of care.” The administration of both puberty blockers and exogenous hormones supported their evolution from a transgender pre-pubertal child to a transgender adolescent with synchronicity between body and psyche, avoiding an unwanted puberty and instead providing a puberty more in line with their affirmed gender.
2. *Pubertal presentation – treated*: This group includes peri-pubertal adolescents and young adults who have recently been identified as exhibiting gender dysphoria that began with the onset of puberty. These individuals present with a developmental history that indicated no gender identity questioning and often no expansive gender expressions prior to puberty. However, they became distressed or stressed about their gender with the onset of adolescence and the physical changes resulting from secondary sex

characteristics development. After careful monitoring and evaluation, some of these youth may begin their endocrine care with puberty blockers to stall any further development of puberty if they are still only in early Tanner stages of puberty, followed by hormone therapy. Some may have already completed their endogenous puberty when their gender stress or distress first surfaces and therefore may begin their endocrine care with hormone therapy or with the administration of puberty blockers in preparation for hormone therapy or concurrent pubertal suppression and hormone therapy.

3. *Postpubertal presentation – untreated*: Another group of presenting gender dysphoric youth may not have received endocrine gender care until they arrive at an adult clinic for reasons such as barriers to seeking care (e.g., lack of access to gender-affirmative pediatric programs; prohibitive financial costs, particularly for puberty blockers; refusal of insurance companies to cover the cost of gender-related endocrine medical interventions for a minor; refusal of their parents to consent to such services for their minor-age child), their choice to postpone hormone therapy until they are assured of full reproductive capacity, or their desire to take time to investigate both the effects and the risks of hormone therapy before engaging in an only partially reversible treatment. This group includes young adults who began questioning their gender in adolescence and are continuing to do so into adulthood, with no history of any gender-affirming medical interventions but with prior visits to an endocrine program for consultation and evaluation. Some of these individuals are still in process of exploring their gender and determining what, if any, medical interventions they might consider in consolidating their authentic gender selves.

Among all of these groups will be the rapidly expanding category of non-binary young people, who identify as neither male nor female but perhaps both or all and any. Such peri- and postpubertal patients will be considering, for example, perhaps a “touch of testosterone” but not a full course, or a

“hit of estrogen,” and are still in the midst of that process as they graduate from pediatric to adult care. Unfortunately, some of these youth may have requested interventions but have been turned down by pediatric endocrine programs because of the discomfort of prescribing hormones to someone whose gender is neither male nor female or as a result of requests that are negatively perceived by some providers as a “boutique” package of endocrine services. Providers’ discomfort is alleviated through continuing education on non-binary identities and individualized hormone treatment plans.

Treatment and Screening Recommendations

Historically, and even in present day, many clinicians have been operating under the assumption that all transgender patients had a binary gender identity (e.g., man or woman only) and desired to “fully transition” and “blend in” as if they were cisgender (i.e., not transgender). While this may be true for some binary transgender patients, it is not true for all transgender patients and should not be assumed. Instead, a gender-affirmative patient-centered approach that is individually tailored to meet each patient’s unique needs and that does not make assumptions about patients’ gender identities or treatment goals for gender care is recommended [3].

Many of the individuals in the early childhood onset group receive endocrine care for gender as early as 9 years old, with their first visits to an interdisciplinary gender clinic pre-dating that by as much as 4–5 years. Those in the second group will most likely have started their endocrine care at the onset of puberty and beyond, and some of those in the third group could have had many years or only a few in the care of a pediatric gender clinic before graduating to adult services.

Some of these young adults socially transitioned at an early age and received puberty blockers at Tanner stage 2 of puberty and then hormone therapy. Their needs for adult endocrine care are simply continuity of care. For example, a 19 year-old transgender man, who socially transitioned

at age 9, presents for a refill of testosterone cypionate and asks if his “T level” is in the normal range for a 19 year-old male. Assuming he was closely followed, this patient would have never menstruated or experienced significant breast development.

By early adulthood, many of these youth, especially those who have not been able to access desired endocrine treatments, experience significant body dysphoria. They agonize about being misgendered by people who do not recognize them for the gender they are [12, 13]. They may feel blocked in their sexual development, inhibited to pursue romantic interests because their body feels so out of sync with their gender identity, and fear rejection from a potential partner who would be repelled by their body. Many grieve the inability to give birth to a child or to impregnate a partner. Lastly, these young people often experience self-hatred and are loathe to look in the mirror at a body that feels so discordant to them.

Those who have the opportunity to receive either puberty blockers and/or hormone therapy in adolescence may still experience substantial anxiety and stress when they enter adult endocrine services, often due to the desired effects of hormone treatment falling short of expectations. Patients often find themselves continuing to suffer from body dysphoria that they thought would disappear as hormone therapy took effect.

Young adults who wanted but were unable to access puberty blockers or hormone therapy during adolescence may present as frustrated and angry when they enter adult endocrine care. Often, either one parent or both parents would not consent or doctors refused to treat, because of the patient’s young age and the medical professional’s probable lack of training and experience in treating transgender young people. Some parents are not comfortable making decisions about their child’s gender and ask their children to wait until they reach the age of majority to seek treatment on their own accord, resulting in patients who feel desperate for services when they reach adulthood. Many people, particularly those

who do not accept that any youth should transition from one gender to another, assert that it is irresponsible to provide youth partially irreversible (hormone therapy) or completely irreversible (surgery) interventions because the frontal cortex of the brain does not fully develop until age 25. This is in contrast with other societally accepted milestones, such as driving or joining the military, which occur well before age 25. Withholding treatment from patients with gender dysphoria is a choice that has the potential to cause harm to these patients [14].

The UCSF Center for Excellence for Transgender Health presents updated and comprehensive primary care guidelines which include an overview of available medical and surgical options, as well as comprehensive information regarding medication preparations and laboratory recommendations for initiating and monitoring GnRH analogues and hormone therapy [15]. The guidelines state, “While the current Endocrine Society guidelines recommend starting gender-affirming hormones at about age 16, some specialty clinics and experts now recommend the decision to initiate gender-affirming hormones be individually determined, based more on state of development rather than a specific chronological age” [16]. This approach is becoming more commonplace among experienced primary care and endocrine providers in the United States.

Medical gender care includes pubertal suppression, feminizing hormone therapy, and masculinizing hormone therapy [17,18]. Medications for pubertal suppression and suppression of endogenous sex hormones in postpubertal adults include gonadotrophin-releasing hormone (GnRH) agonists such as leuprolide or histrelin. These medications have been challenging to access, as insurance companies routinely deny coverage. Persistence on the part of the provider and team has proven effective in these situations. Feminizing hormone therapy includes a regimen of both anti-androgen and feminizing hormones. Spironolactone is most commonly used to suppress endogenous androgens, and finasteride is also recommended. Some patients may still be treated with GnRH

agonists to suppress endogenous androgens with the intent of ending GnRH therapy after gonadectomy. Currently, 17-beta estradiol is recommended, and conjugated estrogens and ethinyl estradiol/oral contraceptives are not recommended due to difficulties with accurately measuring blood levels. Adding progestins to feminizing regimens remains an open question as no professional consensus exists as to their use. Anecdotal reports from providers and transgender women include increased breast development and improved mood. The goals of masculinizing hormone therapy can generally be achieved by parenteral testosterone. Patients tend to prefer subcutaneous routes of injection because of the smaller needle and reduced chance of scarring from long-term use. Injectables tend to be more affordable and produce more potent effects than transdermal preparations. Occasionally progestins may be prescribed initially to suppress menstrual bleeding in the short term or for contraceptive purposes in the long term.

Mental health benefits associated with hormone therapy, including reducing depression and anxiety as well as improving quality of life, have been demonstrated among transgender patients [19–21]. While mental health providers are a necessary part of the treatment team, requiring that patients participate in therapy in order to access gender-affirming medical care is not recommended. This forces mental health providers into a gate-keeping position, which does not foster trust or open communication between patients and therapists. Because of the stressors associated with transitioning and being a transgender person in a non-accepting world, therapy with skilled gender mental health providers can help connect young people to supports, foster resilience, increase coping skills, gain skills and confidence around dating, and decreased self-hatred. Family therapy may be helpful in cases where the patient lacks family support. Therefore, discussions of therapy need to occur routinely during adolescence and young adulthood. However, finding trained gender-affirmative mental health providers is often challenging due to lack of trained providers in the area or financial restrictions.

In best practices, youth in the second group above pubertal presentation, are advised, that puberty blockers at Tanner stage 2 directly followed by masculinizing or feminizing hormones will, under present medical standards, render that youth infertile. Early childhood onset youth, in the first group above, who may never have received endocrine care, either puberty blockers or hormone therapy, need counseling about gamete preservation, whether they will choose to store sperm or eggs or embryos before initiating hormone therapy. For many young adults, this continues to be a developmental disruption, one that adult endocrinologists should be aware of: gender providers encourage young adults to consider fertility, often in direct contrast to advice they receive from others to avoid having a baby until later, when they have either completed post-secondary education or have more securely established themselves financially.

Healthcare Process

While many transgender youth who transfer from a pediatric provider to an adult provider have received care from an interdisciplinary specialized gender clinic, many others have received care from a non-specialist pediatrician. For transgender young adults, the treating provider's level of training, experience, and connection with the transgender community is more important than the particular specialty. However, specialty endocrinology care may be necessary in certain cases, for example, when other providers have difficulty getting patient's hormone levels to the desired range or if the patient has a co-occurring endocrine disorder.

Pediatric clinics are reporting that many young adults choose to continue care for several years with their pediatric gender service, if that program allows extension into early adulthood. They typically do this for one of two reasons: (1) the comfort with and trust in the providers with whom they have established a strong relationship, some for many years, and (2) the availability of wrap-around services, including

mental health services, family and group supports, legal consultation, and educational advocacy that are often part of pediatric, but not adult gender programs. Others are eager to move to an adult program which may feel more developmentally appropriate and may be more likely to provide care based on informed consent rather than requiring extensive evaluations or letters of readiness/support. Others will transition simply because they are no longer eligible for the pediatric program.

Endocrinologists' practical knowledge of common issues with the physical exam with transgender young adults will optimize the transition process. First, providers should be aware that the language used for patient's primary and secondary sex characteristics is important for developing rapport and trust with transgender patients. Providers can best serve these patients by asking the patients how they would like you to refer to their chest and genitals before conducting these exams. For example, a provider might ask a patient, "I understand that different people use different words for their genitals and I would like you to be comfortable. What words would you like me to use?" Next, as body dysphoria may manifest in extreme distress surrounding the physical exam, especially for inspection and examination of primary and secondary sex characteristics, patients may require an increased level of sensitivity around breast and genital exams. Some patients may outright refuse them. For patients that do consent, providers should take care to ask permission and explain what they are going to do before touching the patient. Care and compassion should be demonstrated by the provider during these exams, and they should only be done if medically necessary. For trans masculine patients who cannot tolerate internal vaginal exams, less invasive alternatives such as transabdominal ultrasounds should be offered. Further, as they inspect patients during the physical exam, providers should be aware that some patients use non-medical silicone injections in their breasts, hips, face, etc. Nonjudgmental and open discussions with expressions of care and concern about previous use of non-medical silicone will encourage patients

to share their history honestly. Patients may or may not desire their endocrinologist to measure changes related to hormone therapy during the physical exam. Historically, some providers have routinely measured breast development for feminizing patients and clitoral growth for masculinizing patients. Before engaging in these measurements, explain why you would do these measurements (e.g., to keep record of the effects of hormone therapy), let them know that it is optional, and ask the patient if this is something they desire.

During the physical exam, providers should know that transgender patients commonly wear specialized items that aid in their gender presentation. Trans masculine patients who have breast development may wear a chest compression binder to diminish the appearance of their breasts and to help decrease the experience of chest dysphoria. Some patients who do not have access to binders may use ace bandage wrap or duct tape to flatten their chest. Trans feminine patients who have not achieved their desired level of breast development may wear bras with breast forms to enlarge the appearance of their breasts. As chest/breast dysphoria in these patients may be significant, asking a new patient if they would prefer to delay the physical exam until the next appointment may help increase patient trust and comfort with the provider. Due to extreme chest/breast dysphoria, some trans patients may refuse to take off their binder or bra. A calm and patient explanation of why you are asking the patient to remove these items (i.e., to inspect for rashes or yeast infections under their breast tissue, to view chest expansion on exhalation, to auscultate for heart sounds, or to examine breast for masses, etc.) may encourage patient participation. Creative solutions, such as having the patients place the stethoscope under their binder themselves or having the patient place their hand on top of your hand during breast examination, can prove effective. Patients who desire to diminish the appearance of their penis may wear specialized undergarments called gaff underwear, which aid them in a process called tucking (i.e., pulling the penis toward the anus and separating the testicles to produce the appearance

of a flat front). Some patients also push their testicles up the inguinal canal on each side in order to further reduce their genital bulge. Because of this form of tucking, they might have defects or a hernia at the external inguinal ring. Trans masculine patients may wear “packers” in their underwear to create the appearance of a penis. Some will be able to use their packer to urinate while standing. As packers may come in direct contact with patient’s genitalia, a discussion of methods and frequency of cleaning their packer(s) may be helpful.

Knowledgeable and nonjudgmental sexual history taking with transgender young people is of paramount importance. Like with the physical exam, use of individualized and affirming language encourages open and honest communication. It is often helpful for providers to consider the gendered wording they typically use, as questions such as “Do you have sex with men, women, or both?” may be off-putting to transgender patients, especially those who are non-binary or who have had sex with non-binary persons. After opening with a statement to normalize taking a sexual history, providers might consider letting the patient know that, in order to assess their sexual health, “I need to ask you what parts have gone where and what fluids you have been exposed to.” Open discussions about use of protection that extend beyond condoms for peno-vaginal intercourse are necessary for this population. This may include discussions about dental dams, using condoms on sex toys, and other safer sex practices. Preventive education and counseling on the transmission of sexually transmitted infections (STIs) and HIV are as important with this population as with other adolescent and young adult patient populations. As the risks for STIs and HIV are related to sexual behaviors and not transgender identity, providers should not make assumptions about STI and HIV risk on the basis of the patient’s identity. Instead, risk status is based on sexual behaviors. Patients are more likely to be open and honest about their behaviors if they believe their provider is not making assumptions and responds in a nonjudgmental manner. With regard to discussions around fertility, some patients who have retained their gonads may desire to repro-

duce using their own sperm or ova [22]. Some trans masculine patients will desire to carry pregnancies and may need a referral to an affirming OB/GYN or family practice physician [23]. As uterine transplant becomes available to trans feminine patients [24], it is expected that many of these patients will desire to carry pregnancies as well. Patients may or may not be aware of their own reproductive options or potential and can benefit from open conversations about fertility as well as contraception.

Transgender Specific Transition Considerations

Transgender and gender-expansive young adults qualify as a vulnerable population, much of it stemming from the discrimination, prejudices, and lack of support they receive from the surrounding environment [25]. A primary cause of gender stress is the internal distress when one's body does not feel in alignment with one's gender identity (i.e., gender dysphoria). Research has provided evidence that youth who are supported and accepted in their transgender identities do better psychologically than youth who are not supported [26, 27].

Transgender youth have rates of suicidality, depression, anxiety, and self-harm that are significantly higher than the general population of people their age [28]. Family support, individualized gender transition, and social supports mitigate against these risk factors [27]. Their healthcare is a critical part of that support system. For successful transition, endocrinologists should engage in ongoing efforts to build a network of resource referrals that should include social workers, primary care providers, OB/GYN, hair regrowth and removal specialists, reproductive specialists, substance treatment facilities, surgeons, exercise specialists, nutritionists, psychiatrists, therapists, hair stylists/beauticians, massage therapists, lawyers, and housing resources. This list may seem overwhelming, yet it is daunting for patients who spend countless hours of searching for friendly professionals by

only to encounter discrimination or harassment from professionals along the way. National resource locators such as the Gender Infinity MAP (resource.genderinfinity.org) and RAD Remedy (RADRemedy.org) aid in finding such resources. Another critical part of the patients' support system is their family. The way the family responds to the child's gender transition plays a critical role in determining their mental health outcomes, with increased acceptance predicting better psychosocial outcomes, including decreased suicidality [27, 29]. Endocrinologists can play a critical role in educating family members about gender dysphoria, the importance of affirming their child's gender identity, and how their decision to accept, support, or reject their child has a direct impact on their child's well-being as an adult.

The transfer of care from pediatric to adult endocrine services should be accompanied by an awareness that (1) these youth may need ongoing mental health/psychiatric supports if they are suffering from any of the above mentioned risk factors and (2) it is critical that adult endocrinologists be trained in gender-affirmative approaches to care so that they can become part of the support network rather than the part of the rejecting environment that contributes to the risk factors named above. The gender-affirmative approach, detailed in books [3] and articles [18, 30, 31], includes using the name and pronouns (she, he, they, etc.) that the patient requests, attending relevant trainings, consulting with experts in the field, making sure all office staff are trained in how to provide respectful treatment of transgender and gender-expansive patients (e.g., do not misgender patients, do not ask questions about their gender or body unless you are their provider and have a clinical rationale for asking, etc.), and, at times, advocating for these patients within their healthcare systems and their place of work or education and in political arenas when policies may negatively impact them.

An important isolation-reducing practice is to connect these young adults to groups to meet others like them that are their own age as well as older adults. While many of these young adults will be connected via social media, in practice it

is common to find that many have not met another gender diverse person like themselves in person. Connecting these patients with others like them not only reduces isolation, but it also increases a sense of belonging – thus bolstering resilience against suicidality [32]. In light of the high rates of suicide attempts in transgender populations, the importance of this intervention cannot be overstated. At the same time, it should be noted that some gender diverse young adults, particularly those who may have also been assessed as being on the autism spectrum, may be loath to participate in any group activities; that preference to avoid groups should also be respected.

For groups of dysphoric young adults who were enrolled in treatment before or around puberty, it is important to remember that the exit from adolescence comes with the stresses of being able to make it in the adult world of greater responsibilities, obligations, and requirements of conformity to social norms. Applying this to adult endocrine gender care, it is at this nodal stress point that a mental health professional within an interdisciplinary team becomes essential to good practice, addressing the reality of the young adults' distress while simultaneously facilitating access to resources that will allow the young person to accept the limitations of medical interventions as they build psychological gender resilience.

Finally, when working with transgender young adults, the following practical guides should be kept in mind. First, if you are new to this care, actively seek out supervision, consultation, and training. There are many providers who are members of the World Professional Association for Transgender Health (WPATH) that frequently offer mentorship as new providers see more and more of these patients. Also, since the language and guidelines for care are constantly shifting, it is important to acquire continuing education for treating this population. For example, it is unfortunately common to learn that providers who have been treating patients for years without keeping up with the literature or attending professional conferences have been prescribing too much testosterone or are not prescribing anti-androgen agents and are putting their

patients' health at risk and minimizing the effects patients are seeing from treatment, respectively. Second, the history of transgender care is replete with denials of access to gender-affirming treatment. Actively work with patients to eliminate barriers to care, and provide individualized care that is patient-centered and based on the unique goals of the patient. Third, provide your patients with accurate and up-to-date information on the effects, side effects, and risks associated with gender care. Fourth, work in interdisciplinary teams to provide comprehensive care. This can be in a gender care team or a network spread out over several locations. Fifth, in order to facilitate the transfer to adult care, connect with pediatricians who are providing gender care to young patients, even if they are several hundred miles from your practice. It is very common for patients to travel across state lines to access care.

Key Resources for More Information

At this time, we are not aware of the existence of any materials to support the transition of care process for transgender young people. Several resources for providing transgender care include the USCF Primary Care Protocol <http://transhealth.ucsf.edu/trans?page=protocol-00-00>; the BC Vancouver Coastal Health Primary Care Toolkit <http://www.phsa.ca/transgender/Documents/Primary%20Care%20Toolkit.pdf>; and Tips for Pap Smears with Trans Men http://www.glhv.org.au/sites/www.glhv.org.au/files/Tips_Paps_TransMen_0-1.pdf. Attending conferences not only provides a place for receiving up-to-date education but also can provide opportunities for providers and community members to connect. Professional conferences focused on transgender health include WPATH and USPATH. Annual conferences that focus on professionals and community include Philadelphia Transgender Wellness Conference, Gender Spectrum, Gender Infinity, and Gender Odyssey. Databases of affirming professionals include the previously

mentioned Gender Infinity MAP and RAD Remedy as well as those databases maintained by WPATH and the Pediatric Endocrine Society. Resources produced by professional organizations include WPATH's Standards of Care, which have been in existence since the late 1970s and the current version of the standards is in its 7th edition; and the 2nd edition of the Endocrine Society Guidelines (<https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2017-01658>); and the Pediatric Endocrine Society SIG Position Statement (https://www.pedsendo.org/members/members_only/PDF/TG_SIG_Position%20Statement_10_20_16.pdf).

Lack of provider familiarity with transgender patients and knowledge of the specifics of their medical care creates barriers to the transition process. Practices should make intentional efforts to connect with the transgender community and learn about the specific needs of community in your area at events such as the International Transgender Day of Remembrance. Practices should also reach out to the professional community to increase awareness of the availability of gender care in your area.

As there is a complicated and tense history between the transgender community and medical professionals, it is recommended that each practice seek out and hire transgender team members as well as transgender consultants to assist with the development of services and community outreach. Hiring a transgender patient care navigator who is transgender sends a positive message to the community that the practice values transgender people. In addition, transgender employees will be able to more effectively reach the community and establish trust between community members and the practice.

Conclusion

Transition from pediatric to adult endocrinology is a relatively new terrain for transgender patients and endocrinologists alike, opened up by the advent of puberty blockers for

these youth, followed by hormone treatments, which more and more youth are receiving at younger ages. It is anticipated that guidelines for hormone therapy will focus less on setting a minimum age to initiate treatment and instead on the developmental stage of the patient and individual nature of each case. This shift will only further increase the need for specific practices and resources for transferring care.

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Index

A

- Adult care
 - adult-based transition program, 105
 - chronic endocrine disorders
 - accompanying
 - comorbidities, 106
 - afford medication, 103
 - care coordination, 104
 - continuing education, 104
 - depressive symptoms, 103
 - Got Transition, 104
 - insurance coverage, 106
 - orientation to adult care, 104
 - psychiatric disease and
 - psychological distress, 106
 - routine screening, 106
 - suboptimal self-management behaviors, 107
 - unplanned pregnancy, 107
 - worse disease control, 103
 - patient care paradigms, 98
 - vs. pediatric, 97–101
 - transition care, 101–103
- Adult care models, 52

- Affordable Care Act (ACA) (2010), 43, 44
- American Academy of Pediatrics (AAP), 45, 78
- American Diabetes Association (ADA), 54, 79, 124
- American with Disabilities Act (1990), 8
- Arnett's theory, 4
- Assisted reproductive technology (ART), 150
- Attention-deficit/hyperactivity disorder (ADHD), 143, 144

B

- BC Vancouver Coastal Health Primary Care Toolkit, 214
- Behavioral symptoms, 11

C

- Cancer survivorship, 65, 77, 78, 85, 185, 186, 188
- CARES Foundation, 170
- Chemotherapy, 176, 179–182, 184

- Childhood cancer survivorship
 - childhood brain tumor survivors, 175
 - childhood leukemia and lymphoma survivors, 175
 - developmental and psychosocial issues, 183, 184
 - endocrine dysfunction/infertility, 176
 - endocrine screening recommendations, 177–179
 - endocrine treatment
 - adult-oriented sequelae, 183
 - bone marrow transplantation, 182
 - chemotherapeutic agents, 180, 181
 - hormonal replacement, 183
 - radiation therapy, 181, 182
 - surgical therapy, 179
 - gastrointestinal, renal, cardiac/pulmonary sequelae, 176
 - healthcare process issues, 186, 187
 - hearing/vision impairment, 176
 - morbidity and mortality, 175
 - musculoskeletal abnormalities, 176
 - neurocognitive/psychological abnormalities, 176
 - neurologic dysfunction, 176
 - secondary malignancies, 176
 - transition issues, 185
 - Childhood cancer
 - endocrine care for, 64–67
 - endocrine sequelae of, 26
 - Children's Oncology Group (COG), 176
 - Chronic endocrine disorders
 - accompanying comorbidities, 106
 - afford medication, 103
 - care coordination, 104
 - continuing education, 104
 - depressive symptoms, 103
 - Got Transition, 104
 - insurance coverage, 106
 - orientation to adult care, 104
 - psychiatric disease and psychological distress, 106
 - routine screening, 106
 - suboptimal self-management behaviors, 107
 - unplanned pregnancy, 107
 - worse disease control, 103
 - College Diabetes Network, 128, 132
 - Congenital adrenal hyperplasia (CAH), 26, 33–35, 62–64, 77
 - adrenal enzyme deficiencies, 161
 - classic CAH, 162
 - classic salt wasting, 161
 - CYP21A2 gene mutation, 161
 - developmental and psychosocial issues, 162–164
 - healthcare process issues, 167, 168
 - nonclassical, 161, 162
 - simple virilizing, 161
 - transition
 - guidelines, 168, 170
 - treatment and screening recommendations, 164–167
 - virilizing CAH, 162
 - Cushing's syndrome, 34
- D**
- Diabetic ketoacidosis (DKA), 27
 - Dual-photon x-ray absorptiometry (DXA), 34, 145, 146

E

Emerging adulthood
 adaptation and growing, 4
 anxiety and depression, 13
 apathy and hopelessness, 15
 Arnett's theory, 4
 behavioral symptoms, 11
 change in class/work
 schedules, 7
 chronic endocrine illness, 5
 college campus resources, 7
 comorbid psychological
 disorders, 13
 disability and/or unaware
 legal protections, 8
 federal and state level, 8
 follow-up care, 6
 frontal and limbic systems, 5
 geographic relocations, 7
 health centers, 7
 inform transition-related
 decisions, 15
 lifestyle and psychological
 challenges, 6
 lifestyle behaviors, 9–11
 maintaining anonymity, 7
 mental status alterations, 11
 negative feelings, 14
 neighboring limbic
 structures, 5
 neural systems, 5
 neuropsychiatric symptoms, 11
 one's medical condition, 7
 productivity and energy levels
 changes, 11
 psychiatric disorders, 12
 recentring, 4
 role of family, 15–17
 screening programs, 15
 self-care, 7
 self-confidence and
 self-efficacy, 8
 self-control and resist
 temptations, 5
 sensation-seeking and
 risk-taking behaviors, 5

structural problems, 14
 suicide, 13
 transient mood
 fluctuations, 11
 treatment-related failures, 15
 type 1 and type 2 diabetes, 14
 uncertainty and instability, 4
 unrealistic treatment goals, 9
 Endocrine disorders, screening
 and treatment
 CAH, 33–35
 childhood cancer, endocrine
 sequalee, 35–37
 transgender care, 37, 40
 transgender hormone therapy,
 38–39
 turner syndrome, 30–33
 type 1 and type 2 diabetes,
 26–30
 Endocrine Society guidelines, 35,
 205, 215
 Endocrine Society Type 1
 Toolkit, 128, 129
 Endocrine Society website,
 87, 154

G

Gender expressions,
 196, 200, 201
 Gender identity, 163, 195,
 197–201, 203, 210–212
 Gender Infinity MAP, 212
 Gonadotrophin releasing
 hormone (GnRH), 199,
 205, 206
 Got Transition, 53, 55, 59, 79,
 81–83, 86, 104, 124,
 128, 132

H

Healthcare events, 44
 Health Insurance Portability and
 Accountability Act
 (HIPAA), 40–43

- Healthcare transition models
 adult-focused care, 52
 CAH, 62–64
 childhood cancer, endocrine sequelae of, 64–67
 complete general health management tasks, 53
 identified patient population, 51
 individual and contextual factors, 53
 integration of adolescents, 52
 NCQA recommendations for, 52
 patient-provider relationship strategy, 51
 same health system, 52
 seamless healthcare transitions, 53
 short-term vs. long-term complication prevention, 51
 specialty care settings, 52
 transgender care, 67–69
 transition interventions and novel clinical approaches, 54
 treatment approach, 51
 Turner syndrome, 59–61
 type 1 diabetes
 adult care-based transition programs, 57, 58
 pediatric transition readiness programs, 55, 56
 pre-transition factors, 54
 specialized adolescent and young adult diabetes clinics, 56, 57
 transition interventions, 58, 59
 type 2 diabetes, 59
 Health insurance, 8, 43–45, 66, 67, 78, 87, 119, 185
 Hematopoietic stem cell transplantation therapy, 182
 Hemoglobin A1c (A1c), 118
 Hormonal therapy, 37, 100, 140, 183
 Hypoglycemia, 7, 13, 27, 56, 162
- I**
 Integral themes, 78
 International Society of Pediatric and Adolescent Diabetes' (ISPAD), 124, 127
 International Transgender Day of Remembrance, 215
- K**
 Kieler Modell, 167
- L**
 Let's Empower and Prepare' (LEAP) Program, 56
- M**
 "Moving On" transition program, 56
- N**
 National Committee for Quality Assurance (NCQA), 52–53
 Non-alcoholic fatty liver disease (NAFLD), 121
- O**
 Ovarian tissue cryopreservation (OTC), 150–151
- P**
 Pap Smears with Trans Men, 214
 Pediatric transition care, practical recommendations

- “Got Transition”
 - initiative, 78, 79
 - medical summaries, 87, 88
 - post-transition
 - tracking, 89, 90
 - readiness assessment, 83–85
 - self-care education, 85, 86
 - setting expectations, 80–82
 - transition coordination and referrals, 88, 89
 - transition plan, 86, 87
 - transition
 - preparation, 82, 83
- Post-traumatic stress disorder, 186
- Prader-Willi syndrome, 79
- Primary care practitioners (PCPs), 99, 100
- Privacy laws, 17, 26, 40–43, 45

- R**
- RAD Remedy, 212, 215
- Radiation therapy, 66, 176, 181, 182

- S**
- Sex hormone therapy, 37
- Sexually transmitted infections (STIs), 210
- Socio-ecological model of readiness for transition (SMART), 124
- STARx questionnaire*, 84
- Suicide, 13, 14, 40, 106, 184, 213

- T**
- Testicular adrenal rest tumors (TART), 35, 166, 167
- Thyroid-stimulating hormone (TSH), 121, 178
- Transgender care, 26, 37–40, 54, 67–69, 107, 199, 214
- Transgender hormone therapy, 38–39
- Transgender patients
 - developmental and psychosocial considerations
 - barriers to seeking care, 202
 - early childhood presenters, 201
 - gender expressions, 200
 - gender identity, 200
 - hit of estrogen, 203
 - interdisciplinary approach, 201
 - postpone hormone therapy, 202
 - touch of testosterone, 202
- GnRH agonists, 199
- healthcare process, 207–210
- pediatric gender care programs, 199
- transition considerations, 211–214
- treatment and screening
 - binary gender identity, 203
 - confidence around dating, 206
 - decreased self-hatred, 206
 - fear rejection, 204
 - foster resilience, 206
 - gain skills, 206
 - gender affirmative patient-centered approach, 203
 - GnRH analogues and hormone therapy, 205
 - GnRH therapy, 205, 206
 - hormone therapy, 205
 - increase coping skills, 206
 - masculinizing/feminizing hormones, 207
 - medical gender care, 205
 - mental health benefits, 206
 - puberty blockers/hormone therapy, 204
- Transition readiness assessment questionnaire (TRAQ), 55, 83, 84

- Tucking, 199, 209, 210
- Turner syndrome, 26, 30–33, 59–61, 77–79, 102
- advocacy groups, 145
 - developmental and
 - psychosocial issues
 - academic and vocational functioning, 143
 - adulthood demands
 - appreciation, 142–143
 - day-to-day
 - functioning, 142
 - driving ability, 144
 - except multiplication, 142
 - executive
 - functioning, 141, 143
 - general health, 141
 - hormone-mediated
 - cognitive, 142
 - neuropsychological
 - evaluation, 142
 - nonverbal learning
 - disorder, 142
 - psychosocial challenges, 143
 - psychosocial
 - functioning, 143
 - quantity processing, 142
 - sexual function, 141
 - short stature, 141
 - verbal and visual skills, 142
 - visual-motor/fine motor
 - skills, 141
 - visual-spatial abilities, 141
 - vocational success, 143
 - well-defined cognitive
 - phenotype, 141
 - family and peer support, 145
 - fertility options, 150, 151
 - future health risks, 141
 - healthcare processes, 153
 - hormonal therapy, 140
 - motherhood, alternative
 - options for, 153
 - organizations, 155
 - personal medical history, 141
 - pregnancy, 151, 152
 - primary care providers, 140
 - screening
 - recommendations, 146
 - self-care behaviors, 141
 - social media platforms, 145
 - sub-specialty providers, 140
 - transition guidelines, 154
 - treatment and screening
 - cardiology considerations, 147, 148
 - electrocardiogram and transthoracic
 - echocardiogram, 148
 - endocrinology
 - considerations, 145, 147
 - women health
 - considerations, 149, 150
- Turner syndrome passport, 154
- Turner syndrome Pediatric to Adult Care Transition Toolkit, 154
- Type 1 and type 2 diabetes, 14, 26, 77, 78
- best practices, 125–127
 - developmental and
 - psychosocial
 - considerations
 - A1c value, 118
 - changing diabetes
 - management, 119
 - depressive symptoms, 120
 - diabetes adds
 - complexity, 118
 - family history of, 119
 - health insurance
 - coverage, 119
 - mental health
 - disorders, 119
 - racial/ethnic minority
 - backgrounds, 119
 - risky behaviors, 120
 - sociodemographic
 - stressors, 119
 - healthcare process, 122–124
 - lifelong chronic
 - conditions, 118

transition guidelines
 additional time and support, 132
 assessment and policy, 129, 130
 best practices, 133, 134
 clinical practice consensus guidelines, 124
 Endocrine Society's Type 1 Diabetes Toolkit, 124, 129, 132
 Got Transition, 124, 132
 lower family income, 132
 position statement, 124
 successful transition, benchmarks of, 131
 transfer of care, 130, 131
 transition policy, 127, 129
treatment and screening, 121, 122

U

UCSF Center for Excellence for Transgender Health, 205
USCF Primary Care Protocol, 214

V

Vitamin D replacement therapy, 182

W

World Professional Association for Transgender Health (WPATH), 68, 213–215