RESEARCH REVIEW

AMERICAN JOURNAL OF medical genetics PART A

Healthcare Transition in Patients With Rare Genetic Disorders With and Without Developmental Disability: Neurofibromatosis 1 and Williams–Beuren Syndrome

Andrea Van Lierde,[1] Francesca Menni,[1] Maria Francesca Bedeschi,[2] Federica Natacci,[2] Sophie Guez,[1] Paola Vizziello,[3] Maria Antonella Costantino,[3] Faustina Lalatta,[2] and Susanna Esposito[1]*

[1]Pediatric Clinic 1, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[2]Genetic Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[3]Child and Adolescent Neuropsychiatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Manuscript Received: 1 July 2012; Manuscript Accepted: 10 February 2013

There are between 5,000 and 8,000 distinct rare diseases (RDs) affecting 6–8% of the population, most of which are caused by genetic defects. Many are highly complex, childhood-onset, multi-system disorders that are often associated with developmental disability, and require lifelong, highly specialized care and support. As larger numbers of children with previously fatal RDs survive into adulthood, they encounter significant challenges in transitioning from family-centered, developmentally focused, multidisciplinary pediatric care to a less supportive adult healthcare system that is often unfamiliar with these conditions. This paper discusses the challenges of the transition from pediatric to adult health care in two groups of patients with multisystem genetic RDs (neurofibromatosis 1 [NF1] and Williams–Beuren syndrome [WBS]), and analyzes strategies for making the process easier for patients with and without developmental disabilities. Our findings show that there are still no guidelines in national healthcare programs on how to transition RD adolescents with and without developmental disabilities, and only a few pediatric centers have implemented the elements of transition in their general practice. Evidence regarding programs to facilitate transition is inconclusive and the transition from pediatric medicine to adult medicine for RDs remains a major challenge. However, transition requires both time and personnel, which are difficult to find in periods of fiscal austerity. Nevertheless, we should strongly advocate for governments investing more into transition infrastructure or they will face increased long-term social and economic costs due to poor treatment compliance, disengagement from services, increased genetic risks, and higher rates of disease-related complications.

Key words: adolescents; chronic disease; genetic disorders; neurofibromatosis 1; rare diseases; Williams–Beuren syndrome

How to Cite this Article:
Van Lierde A, Menni F, Bedeschi MF, Natacci F, Guez S, Vizziello P, Costantino MA, Lalatta F, Esposito S. 2013. Healthcare transition in patients with rare genetic disorders with and without developmental disability: Neurofibromatosis 1 and Williams–Beuren syndrome.
Am J Med Genet Part A 161A:1666–1674.

INTRODUCTION

In the European Union (EU), a disease is considered rare when it affects less than one in 2,000 individuals. It is estimated that there are between 5,000 and 8,000 distinct rare diseases (RDs) affecting 6–8% of the population: that is, between 27 and 36 million people in the European Union (EU) [EURORDIS, 2005; Aymé and Schmidtke, 2007]. Most of them are caused by genetic defects, and many are highly complex, childhood-onset, multisystem

Conflict of interest: none.
Grant sponsor: Italian Ministry of Health (Ricerca Corrente, 2011 850/01 Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico).
*Correspondence to:
Susanna Esposito, M.D., Pediatric Clinic 1, Department of Pathophysiology and Transplantation Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via Commenda 9, Milano 20122, Italy.
E-mail: susanna.esposito@unimi.it
Article first published online in Wiley Online Library (wileyonlinelibrary.com): 21 May 2013
DOI 10.1002/ajmg.a.35982

disorders that are often associated with developmental disability, and require lifelong, highly specialized care and support. As larger numbers of children with previously fatal RDs survive into adulthood, they encounter significant problems in transitioning from family-centred, developmentally focused, multidisciplinary pediatric care to a less supportive adult healthcare system that is often unfamiliar with these conditions [Royal College of Paediatrics and Child Health, 2003]. Despite international attention, the problem of transition in patients with RDs with and without developmental disabilities is poorly described in the literature; there are no guidelines in national healthcare programs, and few pediatric centers have implemented the elements of transition in their practices [Reiss et al., 2005; American Academy of Pediatrics, 2011].

In our opinion, transition planning based on the needs of patients should be considered an aspect of standard healthcare and, as it is one of the factors that most influences outcome, it should become an integral part of medical training in order to bring about a change in attitudes in future generations of healthcare professionals. This paper discusses the challenges of the transition from pediatric to adult health care in two groups of patients with multisystem genetic RDs (neurofibromatosis 1 [NF1] and Williams–Beuren syndrome [WBS]), and analyzes strategies for making the process smoother for patients with and without developmental disabilities.

IMPORTANCE OF HEALTH CARE TRANSITION IN NF1

Patient education in self-management and lifelong age-specific monitoring are the cornerstones of managing this cancer-predisposing disease with a wide range of phenotypes (Table I). In the pediatric patient, the healthcare provider faces a series of problem including, for example, screening of early onset complications (i.e., ophthalmologic and orthopedic), growth problems, developmental delay/attention deficit, and managing parents' fear related to the evolving cutaneous and neurobehavioral phenotypes. Yearly clinical genetics evaluation is warranted. In adulthood, disease progression is less protean and the presenting phenotype may influence the rate of the classic annual follow-up. For cutaneous malignant peripheral nerve sheath tumors (MPNST), patients' education is more important than the periodic medical screening, similarly to that occurs for the screening of cutaneous melanoma in the general population. Appropriate sensitization of the patients on symptomatologic "red flags" (such as rapid increase in volume and consistency, intractable pain, sudden/unexplained neurologic symptoms) is the most effective strategy. Periodic/autonomous systemic blood pressure measurements, reproductive issues (i.e., opportunity to molecular confirmation of the diagnosis, prenatal diagnosis aims, and limits), psychologic support related to the severity of the cutaneous phenotype, neuropsychologic evaluation for consequences of the neurobehavioral profile (memory, concentration, etc.) on adulthood activities (i.e., employment) are further topics to be clearly cited. Compliance with scheduled appointments can prevent significant morbidity at an early stage, but even severe neurological malignancies may become symptomatic between appointments [Graf et al., 2006]. Patients should be told which symptoms warrant immediate referral and evaluation, and encouraged to take full responsibility for their disease and report any unusual or recurrent symptom [Ferner et al., 2007].

NF1-affected adolescents and young adults face transition at a vulnerable stage of life because of the more frequent occurrence of complications such as MPNST, which are a major cause of mortality in patients aged 10–20 years [White, 2002; Royal College of Paediatrics and Child Health, 2003; Ferner et al., 2007; Huson et al., 2011; Masocco et al., 2011] (Table II). MPNST and glioma were found to be the two most common causes of reduced life expectancy among NF1 patients. In Kaplan–Meier analyses the median survival for NF1 patients was shown to be 71.5 years, with women living ~7.4 years longer than men [Evans et al., 2011]. On average both men and women lived ~8 years less than their counterparts in the general population. Reduction in life expectancy for NF1 patients was found to be much lower (8 years) than the previously estimated 15-year decrease. However, limitations relating to the underreporting of NF1 on death certificates should be considered.

We suggest that healthcare providers acknowledge the fact that adolescents have a limited ability to evaluate risks and the long-term consequences of their actions, and aim at improving their patients' adherence to self-surveillance by means of information, motivation, and education [White, 2002; Moons et al., 2009; Ginsburg and Carlson, 2011]. A course on communication strategies, as well as educational and behavioral strategies that increase responsibility for self-management and transition decisions, could help professionals to present facts in a balanced manner and foster resilience through positive coping techniques [Giarelli et al., 2008; Miller and Chan, 2008; Ginsburg and Carlson, 2011].

CHALLENGES OF TRANSITION FOR PATIENTS WITH RDS AND DEVELOPMENTAL DISABILITIES: THE CASE OF WBS

WBS patients and their families face many problems in obtaining the care and attention they need, and this is even more difficult in the case of adult patients. As observed in Prader–Willi syndrome [Schrander-Stumpel et al., 2007], their physiological aging may be accelerated. Moreover, as they develop the joint contractures, type II diabetes, obesity, diverticulosis, vascular stenosis, and hypertension typical of the elderly much earlier in their lives (Table I), they have a greater need for hospitalization because of medical complications or surgical interventions [Cherniske et al., 2004; Gordon et al., 2007]. However, there are no specific services for adults with developmental disabilities [Stille and Antonelli, 2004; Sullivan et al., 2011], and hospitalization in adult Internal Medicine, Surgery or Rehabilitation Units may be a considerable challenge because they are reluctant to accommodate patients with developmental disabilities [Royal College of Paediatrics and Child Health, 2003; Bedeschi et al., 2011].

A greater incidence of even severe psychiatric disorders, such as specific phobias, depression, and anxiety that worsen with increasing age, forms part of the characteristic WBS neurobehavioral profile [Howlin and Udwin, 2006; McGorry, 2007; Pober and Morris, 2007; Giarelli et al., 2008; Singh, 2009; Singh et al., 2010; Bedeschi et al., 2011; Sullivan et al., 2011].

TABLE I. Features of Patients With Neurofibromatosis 1 (NF1) or Williams–Beuren (WBS) Syndrome

Features	NF1	WBS
Prevalence	1/3,500	1/7,500–2,000
Genetic defect	Mutation in NF1 gene 17q11.2	Submicroscopic deletion on 7q11.23
Inheritance/mode of transmission	Familial and sporadic/autosomal dominant	Sporadic/autosomal dominant
Age at diagnosis	Pediatric age in most cases	Pediatric age in most cases
Life span	Reduced	Reduced
Main features and complications	Café au lait patches, skin-fold freckling, iris Lisch nodules, cutaneous, sub-cutaneous or plexiform neurofibromas, malignant peripheral nerve sheath tumors, optic pathways glioma, cerebral tumors, gastrointestinal stromal tumors, pheochromocytomas, cardiac and cerebral vasculopathy, hypertension, specific bony dysplasia (thinning of the long bone cortex, sphenoid wing dysplasia), scoliosis	Developmental disorder, cardiac malformations in 75% of cases (mainly supra-valvular aortic stenosis), facial dysmorphism, strabismus and/or refractive disorders, hyperacusis, subclinical hypothyroidism, diabetes, obesity, hypertension, joint contractures occurring early in life
Cognitive impairment	Rare (mean IQ in the low 90's) although more frequent than in the general population	Always present, associated with a specific cognitive and behavioral profile
Learning disabilities	40% of patients ± ADHD[a]	70% of patients
Progression of clinical picture	Yes	Yes
Healthcare needs in infancy and childhood	Neurodevelopmental and ADHD screening; ophthalmological, dermatological, orthopedic treatment; abdominal ultrasound scan; blood pressure measurements; other clinical/instrumental evaluations when clinically necessary	Neurodevelopmental, psychiatric, cardiovascular, nephrological, orthopedic, ophthalmological, gastrointestinal, audiological, and odontostomatological treatment
Healthcare needs during adolescence	Neuropsychiatric, ophthalmological, dermatological, orthopedic treatment; abdominal ultrasound scan; blood pressure measurements, other clinical or instrumental evaluations when clinically necessary	Neurodevelopmental, psychiatric, cardiovascular, nephrological, orthopedic, ophthalmological, gastrointestinal, audiological, and odontostomatologic treatment
Healthcare needs in adulthood	Clinical evaluations; blood pressure measurements and neurological evaluations; other clinical or instrumental evaluations when clinically necessary	Clinical evaluations; cardiovascular, endocrinological, dietary, nephrological, orthopedic, ophthalmological, gastrointestinal, audiological, and psychiatric evaluations; other clinical or instrumental evaluations when clinically necessary
Frequency of health controls in infancy and childhood	Yearly	Yearly
Frequency of health controls in adulthood	Yearly	Twice a year
Reproductive fitness	Normal	Greatly reduced
Psychological needs	Patients	Patients, caregivers

From Ferner et al. [2007] and Bedeschi et al. [2011].
[a]ADHD, attention deficit hyperactivity disorder.

TABLE II. Transition Problems in Patients With Neurofibromatosis 1 (NF1) and Williams–Beuren (WBS) Syndrome

Concerns and needs of patients at transition	NF1	WBS
Need of a caregiver in adulthood	No	Yes
Education in the disease and self-management	Yes	Yes (caregiver and patient)
Sexuality and contraception	Yes	Yes (caregiver and patient)
Genetic counseling	Yes	Yes (caregiver and patient)
Autonomy issues	No	Road map to autonomy
Social integration	Related to disease severity	Actively promoted
Academic goals	Average	Limited
Employment	No special requirements	Supported
Insurance coverage, disability certification	Yes	Yes
Guardianship/Trust fund	No	Yes
Recommended age at transition	16–20 years	Depending on developmental age
Compliance with clinical planning	Patient related	Parents/caregivers related
Compliance with treatment and scheduled appointments	Patient related	Parents/caregivers related
Physical therapy	No	Yes
Psychological/psychiatric support	Patient related although more frequent than in the general population	Yes
Dietician	No	Yes
Social worker/vocational counselor/legal assistance	Patient related	Yes
Cultural mediator	Patient related	Patient related

However, diagnosing a psychiatric disorder in young adults with developmental disabilities may be difficult because it may be masked by atypical symptoms or regarded as typical of the underlying condition [Sullivan et al., 2011]. Many patients benefit from ongoing counseling, and a significant subset may require psychiatric assessment/monitoring and medication, but the psychiatric aspects of the syndrome are largely unfamiliar to adult psychiatrists outside specialized centers, and generic mental health services cannot meet the particular needs of these patients [Pober and Morris, 2007; Giarelli et al., 2008; Singh, 2009]. Furthermore, unlike child psychiatrists, adult psychiatrists are not used to providing psychiatric care covering the patients' context, families, healthcare providers, and local social agencies [McGorry, 2007]. A study of adolescents with mental health problems who needed to make the transition to adult services found that those with neurodevelopmental disorders were most likely to remain in child psychiatric care [Singh et al., 2010].

Patients may have difficulties in recognizing and communicating health-related problems of which caregivers may not be aware: for example, problem behaviors might be a symptom of a health-related disorder [Stille and Antonelli, 2004; Schrander-Stumpel et al., 2007; Sullivan et al., 2011]. Furthermore, deficits in visuo-spatial skills, poor concentration and attention, difficulties in dealing with numbers, and problems in fully understanding the requirements of a task can limit a patient's capacity to take responsibility for medical matters. However, the typically good verbal abilities of WBS patients can lead inexperienced adult healthcare providers to over-estimate their general ability and make excessive demands that may cause anticipatory anxiety [Howlin and Udwin, 2006; Bedeschi et al., 2011; Gagliardi et al., 2011]. On the other hand, many adolescents may have considerably fewer adaptive skills than might be expected on the basis of their IQs because they have opposed working on them and their parents have bowed to their wishes [Howlin and Udwin, 2006; Gagliardi et al., 2011].

The challenges of integrating patients in the community are complicated, and caregivers may be concerned that their ability to continue to care for their dependents will be affected by their increasing age. Most WBS patients will continue to need some form of supervision or support in their everyday lives during adulthood, and will go on living with their families or in sheltered accommodation, group homes or residential communities; fewer than 10% will succeed in getting paid jobs [Bedeschi et al., 2011].

The burden of transitioning adolescents with developmental disabilities to adult care lies heavily on the shoulders of family members, whose own psychological needs may be overlooked (Table II). Long waiting lists for adult services, a lack of flexibility in the healthcare system, the stress of coordinating multiple providers, parental working days lost, and difficulties in accessing social benefits, services and support can be overly demanding [Kelly et al., 2008]. We suggest that psychologists and social workers can help by assessing their needs, providing supportive care, acquainting them with their rights to services, and arranging periodic respite at day-care or short-term residential care centers [Kelly et al., 2002; Singh et al., 2010].

MODELS OF TRANSITIONAL CARE FOR SUBJECTS WITH CHRONIC CONDITIONS

Living with a RD affects all areas of life: school, employment, social activities, and affective life [EURORDIS, 2005]. RD patients and their caregivers may have considerable difficulty in finding suitable information about the disorder and identifying experienced adult specialists. Cognitive impairment and psychological problems add to the patients' difficulties in meeting the developmental tasks of adulthood, and challenge the healthcare providers who have assess

their cognitive abilities in adapting to transition [Betz, 2007; Schrander-Stumpel et al., 2007]. In this article, NF1 and WBS (i.e., a cancer prone cognition sparing condition and a disease with marked intellectual disability and a wide range of adult onset complications) were selected because of our experience in healthcare transition with patients affected by these diseases. Currently, we have two research projects regarding NF1 and WBS ongoing after having finished the pilot phase. However, other disease "prototypes" with different disability potentials should be considered. In particular, there are other genetic disorders (such as some bone dysplasias and hereditary connective tissue disorders) with marked physical disability contrasting a nearly normal cognitive development as well as inherited disorders (such as craniosynostoses and some genodermatoses) with severe disfiguring consequences compared with minimal intellectual and physical disability. A further form of disability is that related to genetic conditions at high risk of sudden death (such as hereditary hemorrhagic telangiectasia and Marfan syndrome). Therefore, in RDs in addition to intellectual disability and the need for periodic screening for cancer as major determinants of disability and healthcare transition issues, equally relevant aspects include physical disabilities, social stigma, and fear of death.

There are no guidelines for the management of most RDs, and those that do exist mainly focus on childhood. For example, it is only recently that longitudinal studies of WBS have been published, thus allowing guidelines to be drawn for the care of adult patients [American Academy of Pediatrics, 2001; Cherniske et al., 2004; Howlin and Udwin, 2006; Pober and Morris, 2007; Bedeschi et al., 2011].

In our opinion, both the timing of planning for transition and the steps to be accomplished may be much longer in the case of RD-affected patients. National Health Services and hospital rules set a cut-off for transition at 15–20 years (depending on the country) for practical purposes, but the same rules cannot be strictly applied to patients RDs [Viner, 1999]. Transition goals should be individualized in order to take into consideration their different needs and abilities even if this should mean postponing transition to adulthood [Sowers and Rohland, 2004; Herzer et al., 2010; American Academy of Pediatrics, 2011]. Sexuality and fertility issues, contraception, decisions about whether to have children, alternative options and prenatal diagnoses are especially important in patients with genetic RDs, but may be overlooked in adolescents with developmental disabilities [Sullivan et al., 2011]. Furthermore, social, educational, guardianship, and legal issues must also be addressed. As shown in Tables I and II, uninterrupted healthcare coverage and financial planning should be the expectation and goal [American Academy of Pediatrics, 2002; Schrander-Stumpel et al., 2007; Burdo-Hartman and Patel, 2008; Herzer et al., 2010; American Academy of Pediatrics, 2011].

We suggest that an adult healthcare provider or healthcare team should be identified as early as possible, and their cooperation assured, including the acceptance of caregiver involvement when necessary. Adolescents and their families need physicians who can provide a single point of contact [American Academy of Pediatrics, 2002]. They want to know who will be responsible for their care until the transition is finalized, and what should happen if no adult provider is found [Sowers and Rohland, 2004; Herzer et al., 2010]. Ideally, joint visits should be scheduled to allow adolescents and their families to become familiar with an adult model of care and enable healthcare professionals to exchange information and expertise [Royal College of Paediatrics and Child Health, 2003; Singh et al., 2010].

There are various approaches to the problem of transitioning adolescents with chronic conditions of pediatric onset to adult healthcare (Table III). One involves the transition of adolescents with what are usually considered adult disorders, such as diabetes [Bowen et al., 2010], rheumatological disorders [Shaw et al., 2006] or renal disease [Bell, 2007], to already available adult services. Another involves the transfer of patients with chronic diseases of pediatric onset such as cerebral palsy [Watson et al., 2011] or congenital heart disease [Reid et al., 2004; American Academy of Pediatrics, 2011; Sable et al., 2011] to specialized disease-specific

TABLE III. Requirements for Meeting the Healthcare Needs of RD-Affected Patients at Transition

Expert multidisciplinary team
Availability of dedicated areas
Availability and accessibility of social worker, psychologist, vocational counselor, legal assistance, interpreter, trained nurses, and administrative personnel
Training and education of the transition team
Partnership/joint meetings with adult multispecialist team
Dedicated care/transition coordinator acting as a link to the community
Coordination and information sharing with primary care providers
Telephone time/dedicated lines for patients, families, and primary care providers
Links and collaboration with patient associations
Links and collaboration with other national and international CEs
Capacity to produce and adhere to good practice evidence-based guidelines for RD care in children and adults
Capacity of implementing outcome measures and quality control

CEs, centers of expertise.

centers for adults. Other programs are also disease-based, and allow providers to tailor transition to the particular needs of specific patient groups [Viner, 1999; While et al., 2004; Grosse et al., 2009]. In the United States, national hemophilia and cystic fibrosis network centers routinely provide care for children and adults, thus facilitating the transition [Grosse et al., 2009]. Other models include a transition outpatient clinic [Schrander-Stumpel et al., 2007] or dedicated adolescent multidisciplinary clinics within pediatric or adult services [Royal College of Paediatrics and Child Health, 2003], or integrated teams of pediatric and adult specialists in a pediatric setting [Simon et al., 2009].

Transition programs are poorest where no specific adult services exist, and adult healthcare providers are not trained to care for diseases such as genetic syndromes and metabolic diseases [Viner, 1999; Schrander-Stumpel et al., 2007]. In the medical home model, children with complex multi-organ disorders not only have a source of quality care by a personal physician, but the care is also family-centered and provides easy access to referrals and coordination when needed [Kelly et al., 2002; Lotstein et al., 2005; Burdo-Hartman and Patel, 2008; American Academy of Pediatrics, 2011]. This model may provide an individualized process of transition facilitated by the collaboration of different specialists and the provision of detailed, specific, and written medical information [Kelly et al., 2002]. However, access to a medical home is significantly affected by the severity of a child's condition because the primary care system is less accustomed to providing the coordinated, time-consuming medical, and social care these patients need, or because of poor reimbursement for care coordination [Palfrey et al., 2004; American Academy of Pediatrics, 2005; Gordon et al., 2007; Strickland et al., 2009].

The complexity and low prevalence of RDs require a concentration of resources and expertise that can only be achieved by means of a public health approach. No adequate political support or national RD programs existed in the EU until about 10 years ago [EURORDIS, 2005]. However, since then, there has been an increase in the general awareness of RDs at the level of institutions, public and private organizations, and patient associations, and specific public policies have been developed at national and international level [Aymé and Schmidtke, 2007; Commission of the European Communities, 2008]. Regional or national multidisciplinary facilities specialized in RDs or groups of RDs (Centers of Expertise [CE]) and housed in University-based or tertiary care hospitals have been established in many EU countries in order to ensure high-quality care for RD patients, thus overcoming the limited experience of professionals confronted with very rare conditions [Aymé and Schmidtke, 2007; Rare Diseases Task Force, 2008]. Cross-sectional issues common to different diseases and requiring specific expertise not available at a specific RD center, such as specialized surgery, high-level technology or laboratory services, are managed by specialist centers closely connected with the CEs. Furthermore, local agencies near the place of residence of patients dependent on the public healthcare system may be involved in long-term continuous interventions, such as social, educational and occupational therapy [EUCERD Recommendations, 2011].

CEs cover the multiple needs of RD patients, including RD-related emergency care, by offering support and consultations to the healthcare professionals looking after RD patients, and providing information and guidelines [EUCERD Recommendations, 2011]. They also enable patients and their families to feel less isolated by giving them an opportunity to meet others in a similar situation and exchanging experiences. The primary care providers in this model act as key links between patients, specialized centers, and community clinical and social services, aided by their closeness to the patients' homes, and their better knowledge of the family and local services. It is essential that primary care providers and CEs establish a shared manner of working by mutually exchanging accurate and timely information in order to maintain the continuity of care.

The structure of CEs implies geographical proximity to patients. When CEs for children and adults are located in the same facility, it ensures a relational experience of continuity because the patients are acquainted with the majority of sub-specialists. The transition from child to adult healthcare is less difficult when the patients' multiple needs are coordinated, and common protocols are shared [Gupta et al., 2004; EUCERD Recommendations, 2011]. Transferring information is easier, especially if the same database is used for the clinical follow-up of patients and there are frequent formal and informal contacts between pediatric and adult healthcare providers, and this allows a better view of disease evolution. Not having to change hospitals makes it less problematic for adolescents to move to adult care services, but this would require a widespread network of services providing care and treatment for children and adults with a specific RD, which is impracticable because of the rarity of some diseases and the scarcity of expertise and technology in some areas. Patients living in rural areas or regions in which there is CE for their disease inevitably have to travel to other places to obtain specialized care, and the inverse relationship between the quality of care and the distance from the CE means that this has a high social cost [Aymé and Schmidtke, 2007]. In Italy, CEs for children and adult patients with relatively more frequent RDs such as NF1 are widespread and can be found in different specialties, but not all regions have WBS centers and those that do exist are mainly located in pediatric or pediatric neurology centers [available at http://www.iss.it/cnmr/; accessed March 3, 2012]. Adults with WBS or one of the rarer RDs have to rely on their general practitioner as their main physician and continue to remain in pediatric care even in adulthood. To obviate the lack of specialized CEs in some areas, we think that clinical videoconferencing, telemedicine and tele-expertise facilities could be set up between national and European CEs in order to ensure distant access to the specific healthcare needed [Commission of the European Communities, 2008].

CONCLUSIONS

Although the concept of transition has been generally acknowledged, and a number of position papers and statements have been issued [American Academy of Pediatrics, 2002; Royal College of Paediatrics and Child Health, 2003; Sowers and Rohland, 2004; Stille and Antonelli, 2004; While et al., 2004; American Academy of Pediatrics, 2005; Department of Health, 2006; American Academy of Pediatrics, 2011], there are still no guidelines in national healthcare programs on how to transition RD adolescents with and without developmental disabilities, and only a few pediatric centers have implemented the elements of transition in their general

practice [Reiss et al., 2005; American Academy of Pediatrics, 2011]. Evidence regarding programs to facilitate transition is inconclusive and the transition from pediatric medicine to adult medicine for RDs remains a major challenge.

In our opinion, a successful transition program should include:

- continuing medical education (CME) programs concerning the needs of young adults with RDs, with or without developmental and intellectual disabilities, how to communicate with them, and how to prepare them for self-management and the transition to adult care [Kelly et al., 2002; Moore and Tonniges, 2004; Palfrey et al., 2004; Reiss et al., 2005; Scal and Ireland, 2005; Betz, 2007; Grosse et al., 2009; American Academy of Pediatrics, 2011];
- group discussions between medical students and RD patients and their families;
- training of adult psychologists and psychiatrists in life-span developmental psychology and the management of psychiatric problems in adolescents and adults with developmental disabilities [Beresford, 2004; Scal and Ireland, 2005; Herzer et al., 2010; Singh et al., 2010; Sullivan et al., 2011];
- education and training to healthcare professionals from all disciplines, including paramedical specialists and non-healthcare professionals such as school teachers and caregivers [EUCERD Recommendations, 2011];
- appropriate healthcare resources for RDs [Aymé and Schmidtke, 2007] with financial support to individual CEs allocated on the basis of quality of care evaluations;
- use of smart cards by healthcare services to carry identification and insurance data, and to provide immediate access to a patient's medical history, test results, prescriptions, and information for emergency use [Gupta et al., 2004; Stille and Antonelli, 2004; Kelly et al., 2008; American Academy of Pediatrics, 2011; EUCERD Recommendations, 2011];
- questionnaires asking patients and their families to evaluate their degree of satisfaction and make suggestions for improvement would help to evaluate corrective measures [Viner, 1999; Kelly et al., 2002; Reiss et al., 2005; Herzer et al., 2010].

Transition requires time and personnel, both of which are difficult to find in periods of fiscal austerity. Nevertheless, governments should invest more in transition if they do not want to face increased long-term social and economic costs due to poor treatment compliance, disengagement from services, increased genetic risks, and higher rates of disease-related complications [Herzer et al., 2010; Singh et al., 2010].

Finally, an important discrepancy between the pediatric and adult models of assistance for RDs is represented by the role of clinical geneticist. In pediatric medicine, the role of pediatric clinical geneticist is clear and holistic in nature. In adult medicine, a similar figure is lacking and it is usually assumed by specialists with different core competences and a specialized background. In our opinion, it is important that clinical genetics be an independent medical specialization in all countries and that for adult patients with RDs the clinical geneticist should have a role similar to that of the pediatric clinical geneticist for affected children.

REFERENCES

American Academy of Pediatrics Committee on Genetics. 2001. Health care supervision for children with Williams syndrome. Pediatrics 107: 1192–1205.

American Academy of Pediatrics, American Academy of Family Physicians and American College of Physicians-American Society of Internal Medicine. 2002. A consensus statement on health care transitions for young adults with special health care needs. Pediatrics 110:1304–1306.

American Academy of Pediatrics. 2005. Policy statement. Care coordination in the medical home: Integrating health and related systems of care for children with special health care needs. Pediatrics 116:1238–1243.

American Academy of Pediatrics, American Academy of Family Physicians, and American College of Physicians, Transitions Clinical Report Authoring Group. 2011. Supporting the health care transition from adolescence to adulthood in the medical home. Pediatrics 128:182–200.

Aymé S, Schmidtke J. 2007. Networking for rare diseases: A necessity for Europe. Bundesgesundheitsbl Gesundheitsforsch Gesundheitsschutz 50:1477–1483.

Bedeschi MF, Bianchi V, Colli AM, Natacci F, Cereda A, Milani D, Maitz S, Lalatta F, Selicorni A. 2011. Clinical follow-up of young adults affected by Williams syndrome: Experience of 45 Italian patients. Am J Med Genet Part A 155A:353–359.

Bell L. 2007. Adolescents with renal disease in an adult world: Meeting the challenge of transition of care. Nephrol Dial Transplant 22:988–991.

Beresford B. 2004. On the road to nowhere? Young disabled people and transition. Child Care Health Dev 30:581–587.

Betz CL. 2007. Facilitating the transition of adolescents with developmental disabilities. J Pediatr Nurs 22:103–115.

Bowen ME, Henske JA, Potter A. 2010. Health care transition in adolescents and young adults with diabetes. Clin Diabetes 28:99–106.

Burdo-Hartman WA, Patel DR. 2008. Medical home and transition planning for children and youth with special health care needs. Pediatr Clin North Am 55:1287–1297.

Cherniske EM, Carpenter TO, Klaiman C, Young E, Bregman J, Insogna K, Schultz RT, Pober BR. 2004. Multisystem study of 20 older adults with Williams Syndrome. Am J Med Genet Part A 131A:255–264.

Commission of the European Communities. 2008. Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Rare Diseases: Europe's challenges. Brussels, COM (2008) 679.

Department of Health [DOH]. 2006. Transition: Getting it right for young people. Improving the transition of young people with long term conditions from children's to adult health services. London: The Stationery Office.

EUCERD. Recommendations for Quality criteria for Centres of Expertise for Rare Diseases in Member States. October 24, 2011. Available at: http://www.EUCERD.eu/upload/file/EUCERDRecommendationsCE.pdf Accessed on April 30, 2012.

EURORDIS. 2005. Rare Diseases: Understanding this public health priority. Available at: http://www.eurordis.org Accessed on April 30, 2012.

Evans DG, O'Hara C, Wilding A, Ingham SL, Howard E, Dawson J, Moran A, Scott-Kitching V, Holt F, Huson SM. 2011. Mortality in neurofibromatosis 1: In North West England: An assessment of actuarial survival in a region of the UK since 1989. Eur J Hum Genet 19:1187–1191.

Ferner RE, Huson SM, Thomas N, Moss C, Willshaw H, Evans DG, Upadhyaya M, Towers R, Gleeson M, Steiger C, Kirby A. 2007. Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. J Med Genet 44:81–88.

Gagliardi C, Martelli S, Tavano A, Borgatti R. 2011. Behavioural features of Italian infants and young adults with Williams–Beuren syndrome. J Intellect Disabil Res 55:121–131.

Giarelli E, Bernhardt BA, Mack R, Pyeritz RE. 2008. Adolescents' transition to self management of a chronic genetic disorder. Qual Health Res 18:441–457.

Ginsburg KR, Carlson EC. 2011. Resilience in action: An evidence-informed, theoretically driven approach to building strengths in an office-based setting. Adolesc Med State Art Rev 22:458–481.

Gordon JB, Colby HH, Bartelt T, Jablonski D, Krauthoefer ML, Havens PA. 2007. Tertiary care-primary care partnership model for medically complex and fragile children and youth with special health care needs. Arch Pediatr Adolesc Med 161:937–944.

Graf A, Landolt M, Mori AC, Boltshauser E. 2006. Quality of life and psychological adjustment in children and adolescents with neurofibromatosis type 1. J Pediatr 149:348–353.

Grosse SD, Schechter MS, Kulkarni R, Lloyd-Puryear MA, Strickland B, Trevathan E. 2009. Models of comprehensive multidisciplinary care for individuals in the United States with genetic disorders. Pediatrics 123:407–412.

Gupta VB, O'Connor KG, Quezada-Gomez C. 2004. Care coordination services in pediatric practices. Pediatrics 113:1517–1521.

Herzer M, Goebel J, Cortina S. 2010. Transitioning cognitive impaired young patients with special health needs to adult oriented care: Collaboration between medical providers and pediatric psychologists. Curr Opin Pediatr 22:668–672.

Howlin P, Udwin O. 2006. Outcome in adult life for people with Williams syndrome—Results from a survey of 239 families. J Intellect Disabil Res 50:151–160.

Huson SM, Acosta MT, Belzberg AJ, Bernards A, Chernoff J, Cichowski K, Evans D, Ferner G, Giovannini RE, Korf M, Listernick BR, North R, Packer KN, Parada RJ, Peltonen LF, Ramesh J, Reilly V, Risner KM, Schorry JW, UpadhyayaM EK, Viskochil DH, Zhu Y, Hunter-Schaedle K, Giancotti FG. 2011. Back to the future: Proceedings from the 2010 NF Conference. Am J Med Genet Part A 155A:307–321.

Kelly AM, Kratz B, Bielski M, Mann Rinehart P. 2002. Implementing transitions for youth with complex chronic conditions using the medical home model. Pediatrics 110:1322–1328.

Kelly A, Golnik A, Cady R. 2008. A medical home center: Specializing in the care of children with special health care needs of high intensity. Matern Child Health J 12:633–640.

Lotstein DS, McPherson M, Strickland B, Newacheck PW. 2005. Transition planning for youth with special care needs: Results from the National Survey of children with special health care needs. Pediatrics 115:1562–1568.

Masocco M, Kodra Y, Vichi M, Conti S, Kanieff M, Pace M, Frova L, Taruscio D. 2011. Mortality associated with neurofibromatosis type 1: A study based on Italian death certificates (1995–2006). Orphanet J Rare Dis 6:11.

McGorry PD. 2007. The specialist youth mental health model: Strengthening the weakest link in the public mental health system. Med J Aust 187: S53–S56.

Miller SM, Chan F. 2008. Predictors of life satisfaction in individuals with intellectual disabilities. J Intellect Disabil Res 52:1039–1047.

Moons P, Pinxten S, Dedroog D, Van Deyk K, Gewillig M, Hilderson D, Budts W. 2009. Expectations and experiences of adolescents with congenital heart disease on being transferred from pediatric cardiology to an adult congenital heart disease program. J Adolesc Health 44:316–322.

Moore B, Tonniges TF. 2004. The "Every Child Deserves a Medical Home" training program: More than a traditional continuing medical education course. Pediatrics 113:1479–1484.

Palfrey JS, Sofis LA, Davidson EJ, Liu J, Freeman L, Ganz ML. 2004. The pediatric alliance for coordinated care: Evaluation of a medical home. Pediatrics 113:1507–1516.

Pober BR, Morris CA. 2007. Diagnosis and management of medical problems in adults with Williams-Beuren syndrome. Am J Med Genet Part C (Semin Med Genet) 145C:280–290.

Rare Diseases Task Force. July 2008. European Reference Networks in the field of rare diseases: State of the art and future directions. Third Report. Available at: http://www.rdtf.org. Accessed on April 30, 2012.

Reid GJ, Irvine MJ, McCrindle BW, Sananes R, Ritvo PG, Siu SC, Webb GD. 2004. Prevalence and correlates of successful transfer from pediatric to adult health care among a cohort of young adults with complex congenital heart defects. Pediatrics 113:197–205.

Reiss JC, Gibson RW, Walker LR. 2005. Health care transition: Youth, family and provider perspectives. Pediatrics 115:112–120.

Royal College of Paediatrics and Child Health. 2003. Health services for adolescents: The Intercollegiate Working Party on adolescent health. Bridging the gaps: Health care for adolescents.

Sable C, Foster E, Uzark K, Bjornsen K, Canobbio MM, Connolly HM, Graham TP, Gurvitz MZ, Kovacs A, Meadows AK, Reid GJ, Reiss JG, Rosenbaum KN, Sagerman PJ, Saidi A, Schonberg R, Shah S, Tong E, Williams RG, American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. 2011. Best practices in managing transition to adulthood for adolescents with congenital heart disease: The transition process and medical and psychosocial issues: A scientific statement from the American Heart Association. Circulation 123: 1454–1485.

Scal P, Ireland M. 2005. Addressing transition to adult health care for adolescents with special health care needs. Pediatrics 115:1607–1612.

Schrander-Stumpel CTRM, Sinnema M, van den Hout L, Maaskant MA, Van Schrojenstein Lautman-De Valck HMJ, Wagemans A, Schrander JJP, Curfs LMG. 2007. HCT in persons with intellectual disabilities: General issues. The Maastricht model, and Prader Willi syndrome. Am J Med Genet Part C (Semin Med Genet) 145C: 241–247.

Shaw KL, Southwood TR, McDonagh JE. 2006. Young people's satisfaction of transitional care in adolescent rheumatology in the UK. Child Care Health Dev 33:368–379.

Simon TD, Lamb S, Murphy NA, Hom B, Walker ML, Clark EB. 2009. Who will care for me next? Transitioning to adulthood with hydrocephalus. Pediatrics 124:1431–1437.

Singh SP. 2009. Transition of care from child to adult mental health services: The great divide. Curr Opin Psychiatry 22:386–390.

Singh SP, Paul M, Ford T, Kramer T, Weaver T, McLaren S, Hovish K, Islam Z, Belling R, White S. 2010. Process, outcome and experience of transition from child to adult mental healthcare: Multiperspective study. Br J Psychiatry 197:305–312.

Sowers WE, Rohland B. 2004. American Association of Community Psychiatrists' principles for managing transitions in behavioral health services. Psychiatry Serv 55:1271–1275.

Stille CJ, Antonelli RC. 2004. Coordination of care for children with special health care needs. Curr Opin Pediatr 16:700–705.

Strickland BB, Singh GK, Kogan MD, Mann MY, van Dyck PC, Newacheck PW. 2009. Access to the medical home: New findings from the 2005–2006 National Survey of children with special health care needs. Pediatrics 123:996–1004.

Sullivan WF, Berg JM, Bradley E, Cheetham T, Denton R, Heng J, Hennen B, Joyce D, Kelly M, Korossy M, Lunsky Y, McMillan S. 2011. Primary care of adults with developmental disabilities. Canadian consensus guidelines. Can Fam Physician 57:541–553.

Viner R. 1999. Transition from paediatric to adult care: Bridging the gap or passing the buck? Arch Dis Child 81:271–275.

Watson R, Parr JR, Joyce C, May C, Le Couteur AS. 2011. Models of transitional care for young people with complex health needs: A scooping review. Child Care Health Dev 37:780–791.

While A, Forbes A, Ullman R, Lewis S, Mathes L, Griffiths P. 2004. Good practices that address continuity during transition from child to adult care: Synthesis of the evidence. Child Care Health Dev 30:439–452.

White PH. 2002. Transition: A future promise for children and adolescents with special health care needs and disabilities. Rheum Dis Clin North Am 2:687–703.