

Hard ways towards adulthood: the transition phase in young people with myotonic dystrophy

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Myotonic dystrophy type 1 (DM1), also called Steinert's disease, is a genetic multisystem disorder that has raised, in the last years, high interest because of the high variable clinical spectrum and related disability. Children with myotonic dystrophy are affected by behavioural problems and intellectual disability, finally impacting on their degree of engagement in family, work and social activities. The transition phase, representing the process of moving from adolescence to adulthood, can be severely affected by growing up with a neuromuscular disorder, with significant impact on patient's and families' quality of life. Although conceptual models of health assistance for individual with genetic disorders have already been proposed the burden for the patient and his family is still relevant. Therefore to afford this critical condition it would be suitable to plan proper educational and psychosocial programs, identifying areas of unmet needs and targeted health objectives that ensure the right support to DM1 population.

Key words: myotonic dystrophy, transition, cognitive impairment, neuropsychological impairment

Myotonic dystrophy

Myotonic dystrophy type 1 (DM1), also called Steinert's disease, is a multisystem disorder due to a CTG triplet repeat expansion ([CTG] n) within the myotonic dystrophy protein kinase (DMPK [RefSeq NM_001081563.2]) gene located on chromosome 19q13.3. The main pathogenic mechanisms consists in the deposition of an abnormal transcribed but not-translated RNA from the sequence [CTG] n , within the nuclei of affected cells that express such gene.

In the last years, myotonic dystrophies have been the subject of extensive research because of the high variable

clinical spectrum and related disability. Typically, symptoms become evident during mid-life, but signs can be detectable in the first or second decade; different clinical phenotypes can be recognized based on the age of the affected individual when symptoms first appear: congenital, childhood and classic or late-onset (1).

Congenital DM1, a potentially life-threatening condition at birth, present with hypotonia and severe generalized weakness at birth, often with respiratory insufficiency; severe intellectual disability is also frequent in these children.

Individuals with childhood-onset DM1 develop symptoms between early childhood and early adolescence after a relatively normal birth and infancy, while in classic and adult-onset DM1 forms, symptoms can appear from late adolescence through old age. The disease usually worsen over time, affecting many organs and tissues including skeletal muscle as well as eyes, heart, gastrointestinal tract, endocrine system, and central nervous system (CNS).

There is a general correlation between the degree of expansion and the severity of clinical manifestations (2); an increase of the repeat sizes of the CTG expansions is more frequently associated with female than male transmission (3).

Patients affected by DM1 can be subclassified on the basis of the [CTG] n : E1: 37-150 CTG; E2: 150-1000 CTG; E3: over 1000 CTG (4).

Since the clinical spectrum of different forms of DM1 is highly variable, we will focus on this disease in our forthcoming argumentation, as a complex disease-model in which the *transition* phase can be critical.

Transition in DM1: a bridge from adolescence to young adulthood

In medicine, the *transition* phase indicates the process of changing or moving from one state to another that involves young people aged from 13 to 25; the transition phase usually involves also the families and the professionals living around the patient that *is moving* from being a child to become a young adult.

The definition of transition given actually, grows out of *crisis theory*, the foundations of which were laid by Erich Lindemann's studies (5); according to later investigations by Moos and Tsu (6) "crisis theory asserts that people generally operate in consistent patterns, in equilibrium with their environment, solving problems with minimal delay by habitual mechanisms and reactions. When the usual problem-solving strategies do not work tension arises and feeling of discomfort and strain occur and the individual experiences anxiety, fear, feeling of helplessness, and disorganization". Adolescent psychologist, Erickson (7), explains this crisis is not only the search for a new identity but also a biologically driven physical change. Transition to adulthood for young people, particularly for those affected by a neuromuscular disorder,

means to navigate in a vast range of social frameworks (Fig. 1), at a time of life in which an individual is already vulnerable, whether living with muscle disease or not.

Much empirical work has been done on *human adaptation* to life transitions, showing that individuals are different in their ability to adapt to novelty and change, especially if affected by a chronic disease (8).

Neuromuscular disorders have a high symptom burden and are frequently associated with many adverse psychosocial outcomes, particularly reduced quality of life and impairment in adaptive behaviour (9, 10). A recent work assessed that the psychosocial wellbeing of younger adolescents on degenerative disease trajectories is severely affected by growing up with a neuromuscular disorder, with significant impact on mental health and on levels of engagement in social activities; anyway longitudinal studies are still scarce and there is lack of population based recruitment strategies (11).

It is widely recognized that beyond muscle involvement, DM1 patients present with intellectual, behavioural and emotional impairments, in all the four clinical phenotypes, as a result of central nervous system (CNS) involvement. In the last decades the study of DM1 patients' behaviour became systematic and some authors have re-

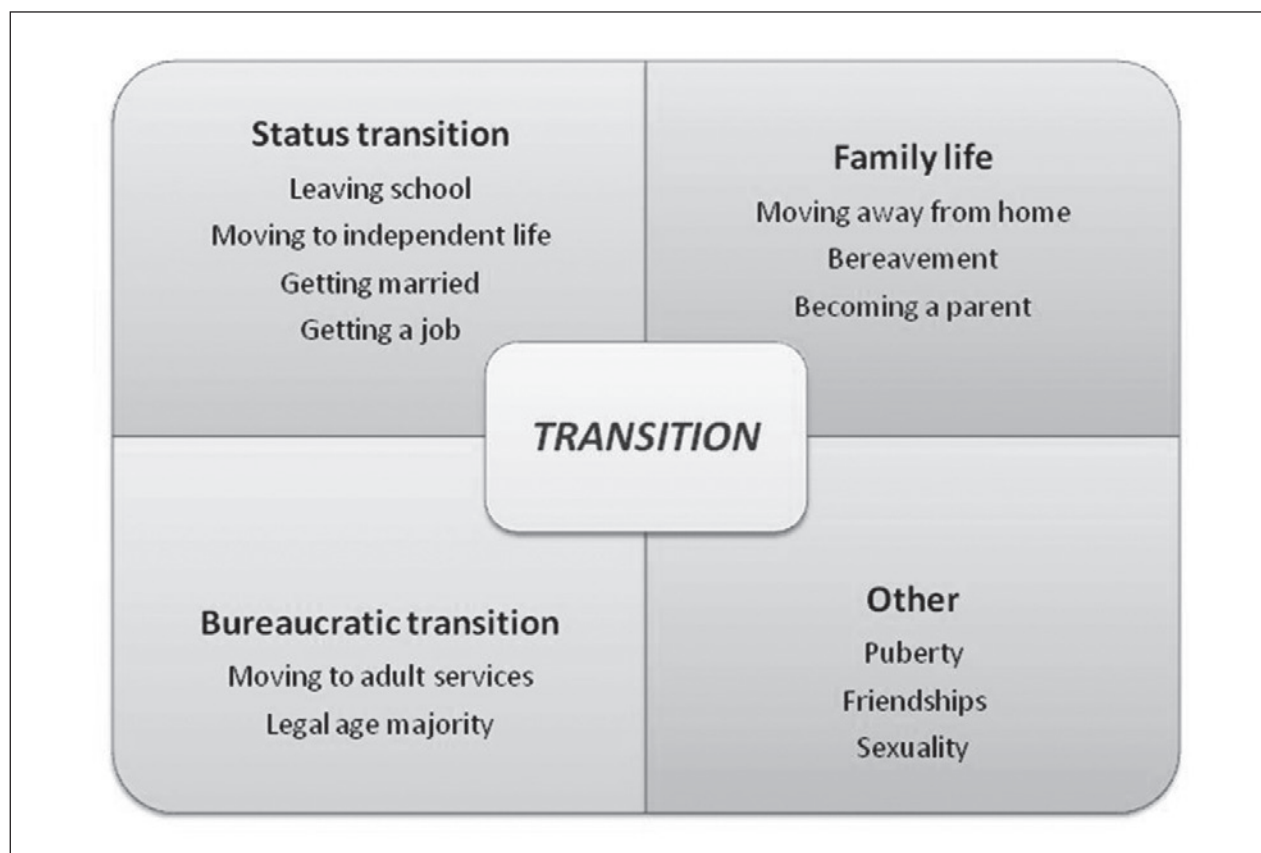


Figure 1. Different social frameworks involved in transition.

ported learning disability to be the most important feature of congenital and childhood DM1 (4, 12, 13), and muscle strength is not pointed out as a major clinical problem, in opposition to the adult-onset phenotype (14); notably, no studies have specifically defined the adult period for the childhood phenotype.

Even if there is no absolute distinction between the different phenotypes the presence and severity of symptoms as well as management issues are quite different from one phenotype to another; in literature while the adult- and late-onset phenotypes have been much studied, publications about the congenital and childhood, especially the long-term outcome, are scarce.

When symptoms develop early in life, this is referred to as congenital or childhood-onset myotonic dystrophy. Currently accepted classifications define congenital myotonic dystrophy patients as having symptoms at birth, whereas childhood-onset myotonic dystrophy patients develop symptoms after birth but before age 10 (4, 15). Children affected by DM1 present learning disability and lower performance in relation to adaptive behaviours, communication and socialization (16); these difficulties in association with lower cognitive functioning hamper participation in playing appropriate social roles while reaching adulthood.

Children with congenital myotonic dystrophy frequently are hypotonic at birth and can have feeding difficulty, respiratory failure, moderate to severe intellectual disability, and autistic features as they age (17). Differently, myotonic dystrophy with childhood-onset can be characterized by development problems, especially intellectual disability and prominent dysarthria (18).

In spite of in the literature the highest prevalence of intellectual impairment is reported in cumulative studies not stratified for the different clinical forms, therefore considering adult and congenital onset of DM1 altogether, it is commonly accepted that congenital form is that one usually characterized by a critical reduction of intelligence quotients in both verbal and nonverbal abilities, as compared to normal control subjects (19-21).

Young DM1 patients can also present with an autism spectrum disorder (ASD), significantly associated with the DM1 phenotype; moreover ASD and/or other neuropsychiatric disorders such as mental retardation, attention deficit hyperactivity disorder, and Tourette's disorder have been found (17), this rising the importance of be aware of behavioural comorbidities in DM1 patients. Interestingly (22) reported that also adult-onset patients with DM1 are affected by social cognitive impairment – commonly defined *theory of mind* (ToM) – that refers to the ability to understand people's mental states, and to establish good relationships in social situations, this suggesting the hypothesis of a continuum between children and adult disturbances in social interaction.

A comparative study highlighted the impact of DM1 symptoms on quality of life, referred by the patients: communication difficulties, cognitive impairment, and social role limitations were the most frequently identified themes, which play a key role in the disease burden (23). However congenital and childhood-onset myotonic dystrophy patients highlighted more learning/concentration difficulties, whereas adult myotonic dystrophy participants were more likely to identify fatigue, reduced motivation and memory deficits as the issues that most affect their lives (24, 25).

Similarly, both populations reported emotional issues; however the congenital and childhood-onset myotonic dystrophy interviews highlighted an inflexibility and a narrow scope of interest in life, aspects not prominently mentioned by adult-onset myotonic dystrophy patients (23).

In a recent attempt to define the portrait of long-term participation in adult DM1 with childhood phenotype (26) the authors showed that behavioural, cognitive, and social stigma problems are related to a guarded prognosis regarding long-term social participation: children affected by DM1 are more likely to rely on social security rather than live independently, and to become isolated in regard to friendship, marriage and having children.

Management of DM1 patients facing transition

Despite the impressive advances in medical care, young people with DM1 are at increased risk for psychological imbalance and social integration difficulties in addition to the burden of motor disability and multisystemic comorbidities; recent evidences show also that a range of symptoms contributing to the burden of disease risk to be under-recognized due to patients' reduced ability to be aware of their difficulties and to some possible bias in caregivers' reports (24, 27, 28).

The complexity of clinical manifestations in this disease pose an important challenge for families and clinicians involved, particularly during the transition phase, in which DM1 patients' management can become fragmented or even deficient, due to a lack of an agreement upon standards of care (29).

Young people and their families have to face a number of issues including:

- lack of continuity in funding, information and expertise in clinical services;
- limited access to education and employment opportunities;
- challenges in their social lives, particularly when forming relationships;
- limited access to appropriate equipment and support for independent living.

Even if new models of health assistance for individ-

ual with genetic disorders have emerged in the last 20 years within public health and education services, still quite high is the burden for the patient to afford critical conditions along the lifespan such as effective transition without proper educational and psychosocial programs; to fill this gap, it is important to explore what is working well and to identify areas of unmet needs, in order to achieve a series of **targeted health objectives** that ensure the right support to DM1 population.

In DM1 **targeted health objectives** can be summarized as follows:

Intellectual disability and cognitive difficulties in domains of attention, memory, visuo-spatial abilities and processing speed, have to be managed integrating specific teaching and supporting strategies into the school setting; the possibility of successful planning relies on the careful planning of a multidisciplinary team (including medical experts in DM1, school personnel and the child's parents).

Communication problems are important in children with DM1; treating clinicians who recognize this issue in patients with DM1 may consider an early referral for speech therapy to reduce dysarthria.

Disease burden: an anticipatory guidance would be suitable to evaluate the possible association between the disease onset and the related disease severity later in life. In this view clinicians should try to alleviate the commitment of follow-up visits, basically boring for young people but still essential to ensure patients well-being as long as possible. Moreover physicians should be constantly aware for the risk ASD and Attention-Deficit/Hyperactivity Disorder (ADHD) comorbidities, that require tailored therapeutic approaches.

Apathy: a child will suffer from a lack of motivation in academic and school-related activities, this suggesting that schools can best help children with chronic illnesses by targeting the mediating variables in the child's environment that affect *motivation* with support of a trained psychotherapist.

Fatigue, irritability, daytime sleepiness may reduce academic and work patients' engagement in hobbies and leisure activities, especially those performed in groups; a step-by-step guidance should be advised to improve patients' ability to be actively involved in groups and emotional control.

In order to achieve the developmental milestones of transition properly, children affected by DM1 need the continuous availability of two main "*educational poles*", the family and the school. According to the Alberta Benchmark Survey (30) parents and teachers have a good understanding of physical milestones, such as when children learn to walk, but are less familiar with important intellectual and social stages. Therefore it could be useful to refer to "psychology of anticipation", a management strat-

egy that has already been postulated to compensate for the potentially harmful effects of any genetic disorder (31). In line with this a medical multidisciplinary team in charge of these patients could be proposed as a "*third educational pole*" in connection with the family and the teaching staff at school, making it suitable that school personnel observe the child's academic functioning and report back to the medical team in a timely fashion. Further assessment by the medical team, in coordination with the school multidisciplinary team, may be necessary to adjust medications, modify treatment schedules, or alter the school day so that the child's academic performance is maximized.

Traditionally the medical care model focuses on treatment of impairments; however, the healthcare process of DM1 patient in transition must be improved not only in terms of assessment of disability but also promoting an action on environmental factors that can be crucial to modify the disability outcome. This can be realized only through an integrated organization of care involving all members of the patients' environment. When properly identified and included in a continuum of care, social and family environmental factors can partly counterbalance existing impairments and disabilities, and avoid the development of handicap situations in life habits.

Conclusions

Transition, indicates the process of changing from one state to another that involves young people aged from 13 to 25; this transition phase, that usually involves also the families and the professionals living around the patient, is a bridge to adulthood that many young individuals find fraught with great difficulty, confusion and profound loneliness. The rapid and numerous changes often characterizing this period may become overwhelming when a young people is affected by myotonic dystrophy.

It would be suitable to define cognitive training programs that may help to potentiate DM1 patients' ability to adapt to novelty and change, focusing on three main endpoints: enhancement of neuropsychological skills, support for mood/personality alterations, self-awareness improvement. The merge of competencies between family, medical and school staff may be beneficial, as a continuous support to cope with disease-related psychological disturbances and motor disability by providing social guidance.

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