Module 4
What clinical phenotypes are seen in myotonic dystrophy type 1 (DM1)?

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Module summary

DM1 presents with varying disease phenotypes across the age continuum[1–3]

*Phenotypes can be categorized as congenital, childhood, adult, or mild/late-onset adult DM1[1–3]**

Congenital DM1 is the most severe form of DM1 and age at symptom onset is <1 month[1,2,4,5]

Newborns typically have complications including hypotonia, immobility, weak cry, respiratory and cognitive difficulties, and EDS[2,3,5,6]

In childhood DM1, age at symptom onset is 1 month–20 years[1]

Children present with subtle facial weakness, cognitive defects, intellectual impairment, psychosocial issues, and incontinence[2]

In adult DM1, age at symptom onset is 20–40 years[1]

Around 75% of individuals develop symptoms in their 2nd–4th decade of life, presenting with highly variable features and multi-organ involvement[4,7]

Mild/late-onset DM1 can occur anytime >40 years of age, and individuals may have fully active lives [1,3]

Individuals often present with mild myotonia, muscle weakness, and cataracts[1,2]

*There is currently no standard on the classifications of DM1.

DM1, myotonic dystrophy type 1; EDS, excessive daytime sleepiness.

1. De Antonio M, et al. *Rev Neurol (Paris)*. 2016;172:572–580; 2. Ho G, et al. *World J Clin Pediatr*. 2015;4:66–80; 3. Bird TD. Myotonic Dystrophy Type 1. 1999 Sep 17 [Updated 2021 Mar 25]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2022; 4. Wenninger S, et al. *Front Neurol*. 2018;9:303; 5. Barbe L, et al. *Am J Hum Genet*. 2017;100:488–505; 6. Lanni S, Pearson CE. *Neurobiol Dis*. 2019;132:104533; 7. Thornton CA. *Neurol Clin*. 2014;32:705–719.

How do clinical phenotypes vary within DM1?

Phenotype*	Age of onset	Clinical manifestations[1,2]	Life expectancy
Congenital DM1[1,2]	<1 month[1]	• Hypotonia • Respiratory distress • Cognitive defects • Motor and developmental delays • Feeding difficulties	45 years† (30–40% mortality rate within neonatal period)[2]
Childhood DM1[1]	1 month–20 years[1]	• Facial weakness • Cognitive defects • Psychosocial issues • Incontinence	~60 years[2†]
Adult DM1[1–3]	20–40 years[1]	• Myotonia • Muscle weakness • Cognitive defects • Cataracts • Conduction defects • Insulin resistance • Respiratory failure	Up to 55 years[3]
Late-onset DM1[1–3]	>40 years[1]	• Mild myotonia • Cataracts	60 years to normal[3]

DM1 presents with varying disease phenotypes across the age continuum[1–3]

*There is currently no standard on the classifications of DM1. †Mean.
DM1, myotonic dystrophy type 1.
1. De Antonio M, et al. *Rev Neurol (Paris)*. 2016;172:572–580; 2. Ho G, et al. *World J Clin Pediatr*. 2015;4:66–80; 3. Bird TD. Myotonic Dystrophy Type 1. 1999 Sep 17 [Updated 2021 Mar 25]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2022.

What are the key features of congenital DM1?

Molecular pathology

- *DMPK* CTG repeat expansion size ≥1,000 almost always due to maternal transmission[1–3]
- Triphasic disease course: severe, global spliceopathy at birth, followed by period of improvement despite large CTG expansions. In adolescence, some maintain improved spliceopathy and others revert to severe spliceopathy[4]

Clinical presentation

- Prenatal symptoms include polyhydramnios and reduced fetal movement[5]
- Neonates are often born preterm with the following distinct complications: hypotonia, immobility, bilateral talipes, contractures, arthrogryposis, facial dysmorphia, hyporeflexia, weak cry, sucking, respiratory and cognitive difficulties, and EDS[2,3,5,6]
- Neonatal symptoms may improve and stabilize, then progress during young adulthood[3,4]
- Intensive intervention at birth is commonly required[7]

Morbidity

- Surviving infants can initially experience gradual improvements in motor function and reach motor and cognitive milestones with some delay; strength typically remains stable until adolescence, when deterioration becomes evident[1,3]
- In young adults, rapid, increasing muscle weakness may occur[3]

Mortality

- 30–40% mortality rate within the neonatal period[3]
- The average life expectancy is 45 years[3]
- Mortality from respiratory failure is common[6]

Congenital DM1 is the most severe form of DM1 and age at symptom onset is <1 month.[1–3,8]
Neonates are often born preterm with distinct neuromuscular, respiratory, and cognitive complications[2,3,5,6]

CTG, cytosine–thymine–guanine; DM1, myotonic dystrophy type 1; DMPK, dystrophia myotonica protein kinase; EDS, excessive daytime sleepiness.

1. Wenninger S, et al. *Front Neurol*. 2018;9:303; 2. Barbe L, et al. *Am J Hum Genet*. 2017;100:488–505; 3. Ho G, et al. *World J Clin Pediatr*. 2015;4:66–80; 4. Hale MA, et al. *Hum Mol Genet*. 2023;32:1413–1428; 5. Lanni S, Pearson CE. *Neurobiol Dis*. 2019;132:104533; 6. Bird TD. Myotonic Dystrophy Type 1. 1999 Sep 17 [Updated 2021 Mar 25]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2022; 7. Johnson NE, et al. *Neurol Clin Pract*. 2019;9:443–454; 8. De Antonio M, et al. *Rev Neurol (Paris)*. 2016;172:572–580.

What are the key features of childhood DM1?

Molecular pathology

- *DMPK* CTG repeat expansion size of >800[1,2]

Clinical presentation

- Children present with subtle facial weakness, cognitive defects, intellectual impairment, psychosocial issues, and incontinence[2]
- Neurocognitive symptoms typically present prominently at around the age 10, and may be recognized earlier than muscular symptoms[1]
- Juveniles may show typical muscular and non-muscular symptoms of adult-onset DM1 (distal weakness, clinical myotonia, cardiac or GI symptoms)[1]

Morbidity

- Children (aged 1–10 years) may have relatively normal motor development early on, and the age of occurrence of the first clinical signs is variable[1,2]
- Juveniles (aged 10–20 years) gradually progress to the adult phenotype, with individuals developing muscular and non-muscular symptoms such as muscle weakness and myotonia, GI symptoms, and cardiac involvement, while retaining the neurocognitive symptoms developed in childhood[1,2]

Mortality

- Average life expectancy of ~60 years[2]

In childhood DM1, age at symptom onset is 1 month–20 years, and individuals present with subtle facial weakness, cognitive defects, intellectual impairment, psychosocial issues, and incontinence[2,3]

CTG, cytosine–thymine–guanine; DM1, myotonic dystrophy type 1; GI, gastrointestinal.

1. Wenninger S, et al. *Front Neurol*. 2018;9:303; 2. Ho G, et al. *World J Clin Pediatr*. 2015;4:66–80; 3. De Antonio M, et al. *Rev Neurol (Paris)*. 2016;172:572–580.

What are the key features of **adult DM1?**

Molecular pathology

- *DMPK* CTG repeat expansion size of 50–1,000[1–3]

Clinical presentation

- Around 75% of individuals develop symptoms in their 2nd–4th decade of life,[4] presenting with highly variable features and multi-organ involvement[3]
- Adult-onset DM1 is often characterized by a combination of symptoms, including facial weakness, ptosis, grip myotonia, and distal muscle weakness with atrophy, cognitive impairment, cataracts, diabetes mellitus, fatigue, EDS, GI disturbances, and cardiac conduction symptoms[1–3]

Morbidity

- Muscle weakness is reported by >45% of individuals with the adult DM1 phenotype[3]
- Chronic respiratory impairment is the primary cause of morbidity[5]

Mortality

- Death typically occurs by 65 years of age[6,7]
- Chronic respiratory impairment is the primary cause of mortality[5]

In adult DM1, age of symptom onset is 20–40 years, and presentation is highly variable[1,3]

CTG, cytosine–thymine–guanine; DM1, myotonic dystrophy type 1; *DMPK*, dystrophia myotonica protein kinase; EDS, excessive daytime sleepiness; GI, gastrointestinal.

1. De Antonio M, et al. *Rev Neurol (Paris)*. 2016;172:572–580; 2. Ho G, et al. *World J Clin Pediatr*. 2015;4:66–80; 3. Wenninger S, et al. *Front Neurol*. 2018;9:303; 4. Thornton CA. *Neurol Clin*. 2014;32:705–719; 5. MDF. Consensus-based Care Recommendations for Adults with Myotonic Dystrophy Type 1.Accessed February 14, 2025. https://www.myotonic.org/sites/default/files/pages/files/MDF_Consensus-basedCareRecsAdultsDM1_1_21.pdf; 6. de Die-Smulders CE, et al. *Brain*. 1998;121:1557–1563; 7. Bird TD. Myotonic Dystrophy Type 1. 1999 Sep 17 [Updated 2021 Mar 25]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2022.

What are the key features of mild/late-onset DM1?

Molecular pathology

- *DMPK* CTG repeat expansion size of 50–150[2,3]

Clinical presentation

- Symptoms generally include mild myotonia, muscle weakness, and cataracts[1,2]

Morbidity

- May have fully active lives[4]

Mortality

- Life expectancy for mild DM1 is 60 years to a normal life span[4]

Mild/late-onset DM1 can occur anytime >40 years of age, usually presenting with mild myotonia, muscle weakness, and cataracts[1,2]

CTG, cytosine–thymine–guanine; DM1, myotonic dystrophy type 1; *DMPK*, dystrophia myotonica protein kinase.

1. De Antonio M, et al. *Rev Neurol (Paris)*. 2016;172:572–580; 2. Ho G, et al. *World J Clin Pediatr*. 2015;4:66–80; 3. Wenninger S, et al. *Front Neurol*. 2018;9:303;
4. Bird TD. Myotonic Dystrophy Type 1. 1999 Sep 17 [Updated 2021 Mar 25]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2022.