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# Advancements and challenges in muscular dystrophy: A comprehensive review of current research and therapeutic approaches

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## Abstract

Muscular Dystrophy (MD) refers to a group of hereditary disorders that are characterized by progressive muscle weakness and degeneration, with Duchenne Muscular Dystrophy (DMD) being the most common and severe form. Despite significant advancements in research and therapeutic strategies, MD remains an incurable condition, presenting substantial challenges for both patients and clinicians. This comprehensive review aims to provide an in-depth overview of the current state of MD research, highlighting recent advancements in genetic therapies, pharmacological interventions, and cell-based treatments. We also examine the challenges associated with these therapeutic approaches, including issues of efficacy, safety, and accessibility. Key areas of progress include gene-editing technologies, such as exon-skipping and CRISPR-based therapies, which have shown promise in restoring dystrophin expression in muscle tissue. Additionally, corticosteroids remain a cornerstone in managing disease progression, although there are concerns regarding their long-term side effects. Stem cell therapies and novel small-molecule drugs also hold the potential for muscle regeneration and symptom relief, although these strategies are still undergoing clinical evaluation. Furthermore, the review discusses the complexities of the clinical trial design, patient stratification, and the necessity for personalized medicine approaches to optimize treatment outcomes. Finally, we address the socio-economic and ethical challenges accompanying new treatments, emphasizing the need for a collaborative, multidisciplinary effort to implement these advancements in clinical practice. This article seeks to provide a comprehensive understanding of the landscape of muscular dystrophy research and therapy, offering insights into promising avenues besides the obstacles that remain in the pursuit of effective treatments.

**Keywords:** Muscular Dystrophy; Duchenne Muscular Dystrophy; Genetic Therapies; Stem Cell Therapy; Pharmacological Treatments; Gene Therapy; Therapeutic Approaches; Clinical Trials

## 1. Introduction

Muscular Dystrophy (MD) refers to a collection of genetic disorders that lead to gradual weakness and deterioration of skeletal muscles. These conditions arise from genetic mutations that disrupt key muscle proteins, causing damage to muscle cells, fibrosis, and a decline in muscle function. MD affects individuals across various ages, genders, and ethnic backgrounds; however, certain types, particularly Duchenne muscular dystrophy (DMD), are predominantly observed in young boys, highlighting the importance of early detection and intervention. There are several subtypes of muscular dystrophy, including DMD, Becker muscular dystrophy (BMD), limb-girdle muscular dystrophy (LGMD), myotonic dystrophy, and facioscapulohumeral dystrophy (FSHD), each with unique genetic causes and clinical features (Bushby *et al*., 2010). Additionally, rarer types, such as Emery-Dreifuss muscular dystrophy (EDMD) and congenital muscular

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dystrophy (CMD), also exist. Duchenne muscular dystrophy, the most prevalent and severe form, is caused by mutations in the dystrophin gene and occurs in about 1 in 3,500 to 5,000 male births globally (Hoffman *et al*., 2015).

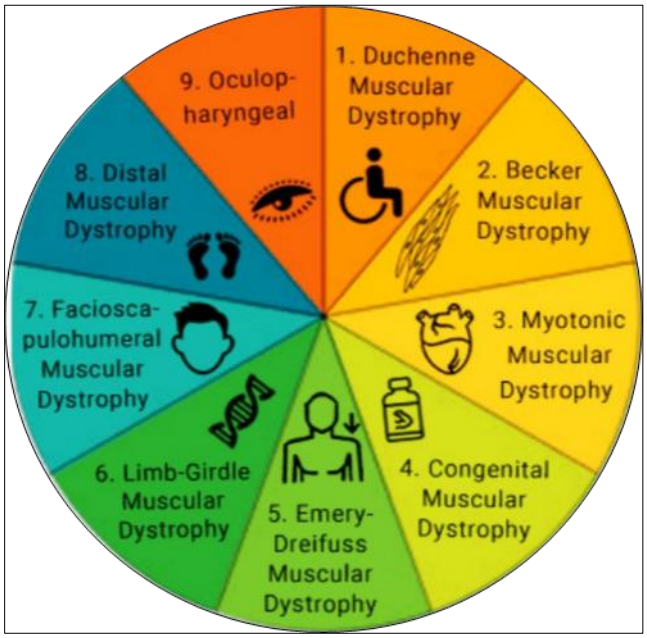


**Figure 1** Types of muscular dystrophy (NeurogenBSI (neurogen_BSI) - profile [Internet]. Pinterest. [cited 2025 Feb 25]. Available from: https://in.pinterest.com/Neurogen_BSI/)

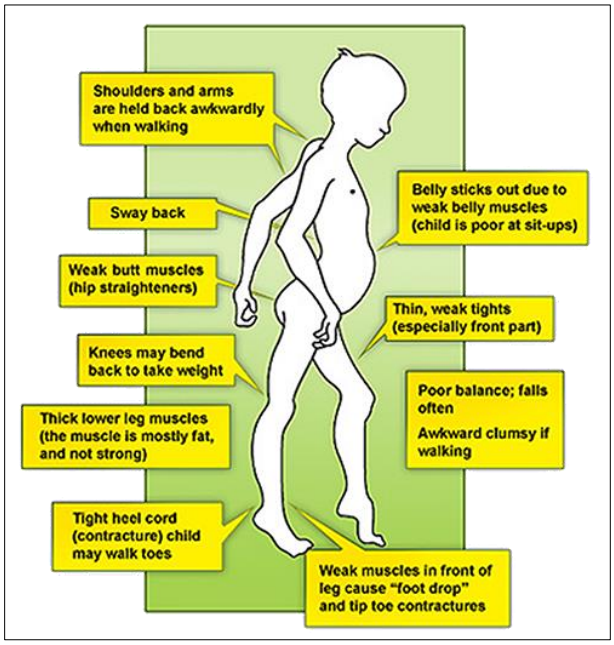


**Figure 2** Symptoms of muscular dystrophy (Treatment and care – are a symbol of Duchenne Canada [Internet]. 🏥 Medicine in Canada 💊. 2017 [cited 2025 Feb 25]. Available from: http://pharmacy-canadian-prices.net/treatment-in-canada/treatment-and-care-are-a-symbol-of-duchenne-canada.html)

Research into muscular dystrophy is vital due to its significant morbidity and the lack of effective treatments. Given the rising global incidence of these conditions, the medical research community must explore the underlying mechanisms and develop suitable therapies (Flanigan *et al*., 2014). The advancement of muscle weakness in MD can lead to mobility loss, respiratory failure, and, in severe cases, premature death. With no definitive cure currently available, muscular dystrophy remains a major focus of research (Mendell & Campbell, 2008). The incidence of Duchenne muscular

dystrophy is approximately 1 in 3,500 male births, and other forms like Limb-Girdle and Facioscapulohumeral dystrophy also significantly contribute to the burden of these diseases (Emery, 2015).

This review highlights key progress in our understanding of muscular dystrophy, including new diagnostic methods and treatment strategies. It also discusses the ongoing challenges in MD research, specifically regarding gene therapy, regenerative medicine, and the variability of genetic mutations across different MD subtypes. Furthermore, it will explore how innovative technologies such as CRISPR-Cas9 and stem cell therapy have created new opportunities for the treatment of muscular dystrophies (Goyenvalle *et al*., 2015).

## 2. Pathophysiology of muscular dystrophy

### 2.1. Genetic basis of muscular dystrophy

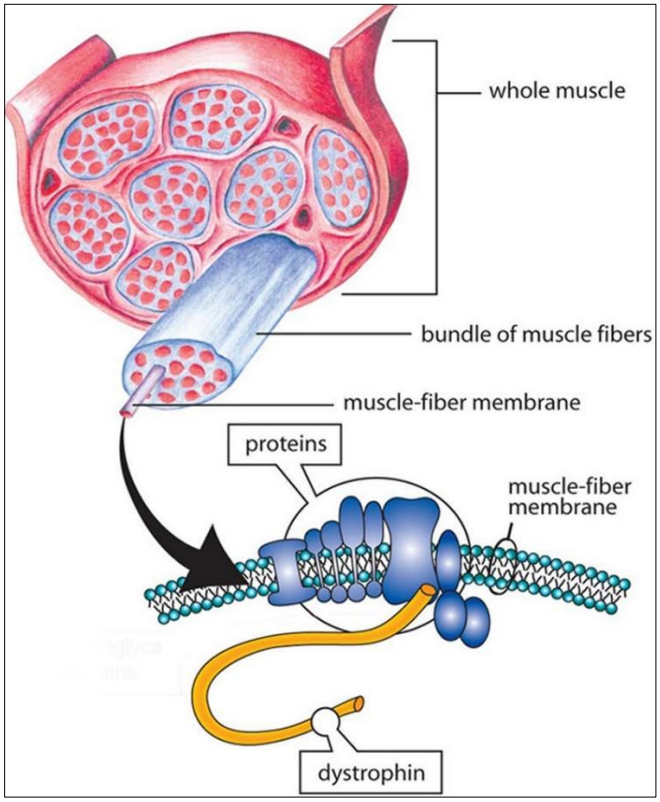


**Figure 3** Dystrophin protein (Muscular dystrophy - causes, types, symptoms, prognosis, treatment [Internet]. Health Jade. 2018 [cited 2025 Feb 25]. Available from: https://healthjade.com/muscular-dystrophy/Muscular Dystrophy (MD) is a group of inherited disorders characterized by progressive muscle weakness and degeneration due to genetic mutations that affect muscle proteins

The primary and most well-studied protein involved in MD is Dystrophin. This protein plays a vital role in maintaining the structural integrity of muscle fibers; without it, muscle cells become increasingly vulnerable to damage. In Duchenne Muscular Dystrophy (DMD), one of the most severe forms of MD, the absence or malfunction of Dystrophin results in fragile muscle cells. These cells are particularly prone to injury during normal muscle contractions and relaxations, leading to a cascade of progressive muscle degeneration. Children with DMD typically begin to exhibit symptoms between the ages of 2 and 6, such as difficulty running or climbing stairs, and this condition predominantly affects boys due to its X-linked inheritance pattern. Becker Muscular Dystrophy (BMD), on the other hand, also arises from mutations in the dystrophin gene but presents with a more moderate severity. In BMD, the gene retains some functionality, allowing for the production of a shortened version of the Dystrophin protein. This partial functionality leads to a milder clinical presentation compared to DMD, with symptoms usually appearing later in life, often in the teens or early adulthood. While both conditions share a genetic basis, the presence of some Dystrophin in BMD accounts for the differences in their observed progression and severity. Moreover, advances in genetic research have uncovered a range of other subtypes of muscular dystrophies, each associated with different genetic mutations. For instance, Limb-Girdle Muscular Dystrophy (LGMD) encompasses a group of disorders linked to mutations in various other genes that encode

proteins critical to muscle function, such as sarcoglycans and calpain-3. These proteins are involved in the muscle cell's ability to withstand stress, and mutations can lead to differing clinical features and rates of progression across the subtypes of LGMD. Beyond DMD and BMD, there are other forms of muscular dystrophy, each with unique genetic causes and varying clinical manifestations. For example, Facioscapulohumeral Muscular Dystrophy (FSHD) is associated with changes in the D4Z4 region of chromosome 4, leading to progressive weakness of the facial, shoulder, and upper arm muscles. As research continues to advance, the understanding of muscular dystrophy—its mechanisms at a molecular level, the specific roles of different proteins, and potential therapeutic strategies—continues to evolve (Flanigan *et al*., 2014). Current studies are exploring gene therapy, exon skipping, and other innovative approaches aimed at modifying the course of these debilitating disorders and improving the quality of life for affected individuals and their families (Zatz & Kunkel, 2010; Saito *et al*., 2018).

In addition to the dystrophin gene, MD encompasses a range of genes and mechanisms that play a role in muscle disease. Limb-Girdle Muscular Dystrophy (LGMD) is associated with mutations in genes like SGCA, which encodes for α-sarcoglycan, and CAPN3, which encodes calpain-3. These proteins are essential for maintaining muscle cell membrane integrity and regulating muscle cell turnover. In myotonic dystrophy, mutations in the DMPK gene lead to a toxic gain-of-function in RNA, causing myotonia and progressive muscle weakness (Mendell *et al*., 2012; Tapscott, 2004).

### 2.2. Molecular mechanisms of muscle degeneration

The molecular mechanisms that drive muscle degeneration in Muscular Dystrophy (MD) are intricate and involve multiple factors, including inflammation, fibrosis, and the apoptosis of muscle cells. Genetic mutations lead to a loss of function in muscle proteins, initiating a series of molecular events that result in muscle deterioration. In Duchenne Muscular Dystrophy (DMD), the absence of dystrophin compromises the muscle cell membrane, making it more vulnerable to mechanical stress and injuries. This damage results in an influx of calcium ions, which activates a series of signaling pathways that incite inflammation, oxidative stress, and muscle fibrosis (McDonald *et al*., 2013). Furthermore, an improperly regulated immune response exacerbates muscle damage, as inflammatory cells invade the muscle tissue, leading to fibrosis and hindering muscle regeneration (Tominari *et al*., 2017; Yoon *et al*., 2015). Chronic inflammation, driven by activated macrophages and T-cells, accelerates muscle fiber damage and limits regeneration. Researchers have also discovered apoptotic pathways that facilitate muscle cell death, especially in the later stages of MD, prompting efforts to create targeted anti-inflammatory treatments to slow the progression of the disease.

As the condition advances, healthy muscle fibers are increasingly replaced by fibrosis and fatty tissue, resulting in further muscle weakness and diminished function. Moreover, muscle regeneration in MD is compromised due to the ineffective activation of satellite cells, which is crucial for muscle repair (Tidball & Wehling-Henricks, 2007). Although some muscle regeneration occurs, it tends to be ineffective because of the buildup of fibrosis and the inability of satellite cells to heal the damaged muscle fibers. These processes are regulated by signaling pathways such as TGF-β, which promotes fibrosis (Mendell & Campbell, 2008).

### 2.3. Differences between various types of muscular dystrophy

There are several different types of muscular dystrophy, each with unique genetic causes, clinical features, and progression patterns. They all share a common feature: progressive muscle weakness and degeneration. Duchenne muscular dystrophy (DMD) is the most severe, typically manifesting in early childhood and progressing rapidly to wheelchair dependence by adolescence and the loss of ambulation by age 12 in most patients. In contrast, Becker muscular dystrophy (BMD) has a milder course, with affected individuals often remaining ambulant into their thirties or forties (McDonald *et al*., 2013). Other types, such as myotonic dystrophy and Limb-Girdle muscular dystrophy (LGMD), have varying genetic underpinnings and clinical presentations (Saugier-Veber *et al*., 2001; Vandenberghe *et al*., 2017). myotonic dystrophy exhibits characteristic muscle stiffness (myotonia) and cataracts, and patients often live longer than those with DMD (Mendell *et al*., 2012).

**Table 1** Types of muscular dystrophy (Understanding Muscular Dystrophy: Types, Symptoms, and Management 0C7 [Internet]. Mavink.com. [cited 2025 Feb 25]. Available from: https://mavink.com/post/D06E01611F43FF532A11E7C7120770383CAM0C7749/muscular-dystrophy-types-chart)

| Type | Symptoms | Age of Onset | Affected Muscles | Prognosis |
|---|---|---|---|---|
| Becker | Weakening muscles. Affects only males | Between 2 and 16; up to 25 | Affects arms legs and spine, can cause heart problems | Can live into adulthood |
| Congenital | Weakening muscles, joint stiffness, and shortening of muscles. | Presents at birth | Primarly affects many voluntary muscles | Progression varies. Can shorten lifespan |
| Duchenne | Weakening of muscles. Can also cause breathing issues and/or heart issues. Affects only males. | Usually appears between the ages of 2 and 6 | Affects arms, legs, and spine. | Fast progression. Usually live until teenage years or early 20s. |
| Emery-Dreifuss | Causes muscle weakening in upper arms and lower legs | Anytime between childhood and teenage years | Upper arms, lower legs, chest, shoulders | Slow progression |
| Facioscapulohumeral | Difficulty walking, chewing and speaking | Usually between teenage and early adult ages | Face, shoulder blade and upper arms | Slow progression |
| Limb-Girdle | Weakening in hips, shoulders, arms and legs | Teens to early adulthood | Hips, shoulders, legs and arms | Medium progression. Typically live to middle adulthood |
| Myotonic | Stiffening and spasms of muscles | Anytime from childhood to adulthood | Overall muscle weakening, can also affect central nervous system. | Slow progression, decreased life expectancy |
| Oculopharyngeal | Weakening in eye and face muscles | Appears between 40-60 years old | Face muscles and possibly pelvic and shoulder muscles | Slow progression |
| Distal | Causes weakening in distal muscles | Appears during adulthood | Affects distal muscles such as hands, feet, and lower legs | Slow progression and less severe than other forms |

## 2.4. Current diagnostic approaches

### *2.4.1. Genetic testing*

Genetic testing has become a cornerstone of MD diagnosis. Next-generation sequencing (NGS), polymerase chain reaction (PCR), and microarray techniques have revolutionized the detection of mutations in key genes, enabling more accurate and earlier diagnosis (Mazzone *et al*., 2011). PCR amplification is still used for detecting common mutations, such as exon deletions in the DMD gene. In particular, the advent of NGS has enabled comprehensive genetic screening for multiple forms of MD in a single test and for identifying genetic heterogeneity (Flanigan *et al*., 2014), improving diagnostic efficiency and helping clinicians identify the specific mutation responsible for the disease (Wilmshurst *et al*., 2019). Early genetic diagnosis is crucial, as it enables timely intervention, which can delay disease progression and improve quality of life.

*2.4.2. Imaging techniques*

Imaging techniques such as MRI and muscle ultrasound are increasingly used to monitor disease progression and assess muscle involvement in MD patients. MRI, in particular, has become an essential tool for detecting fat infiltration in muscle tissue, which is a hallmark of disease progression in MD (Bashir *et al*., 2006), allows for the non-invasive assessment of muscle degeneration, and is being used in clinical trials to assess the efficacy of new therapies (McDonald *et al*., 2013). Muscle biopsy, although less commonly used due to the invasiveness of the procedure, remains a diagnostic gold standard, allowing for histopathological examination of muscle tissue to assess muscle damage and the extent of inflammation or fibrosis (Passamano *et al*., 2012).

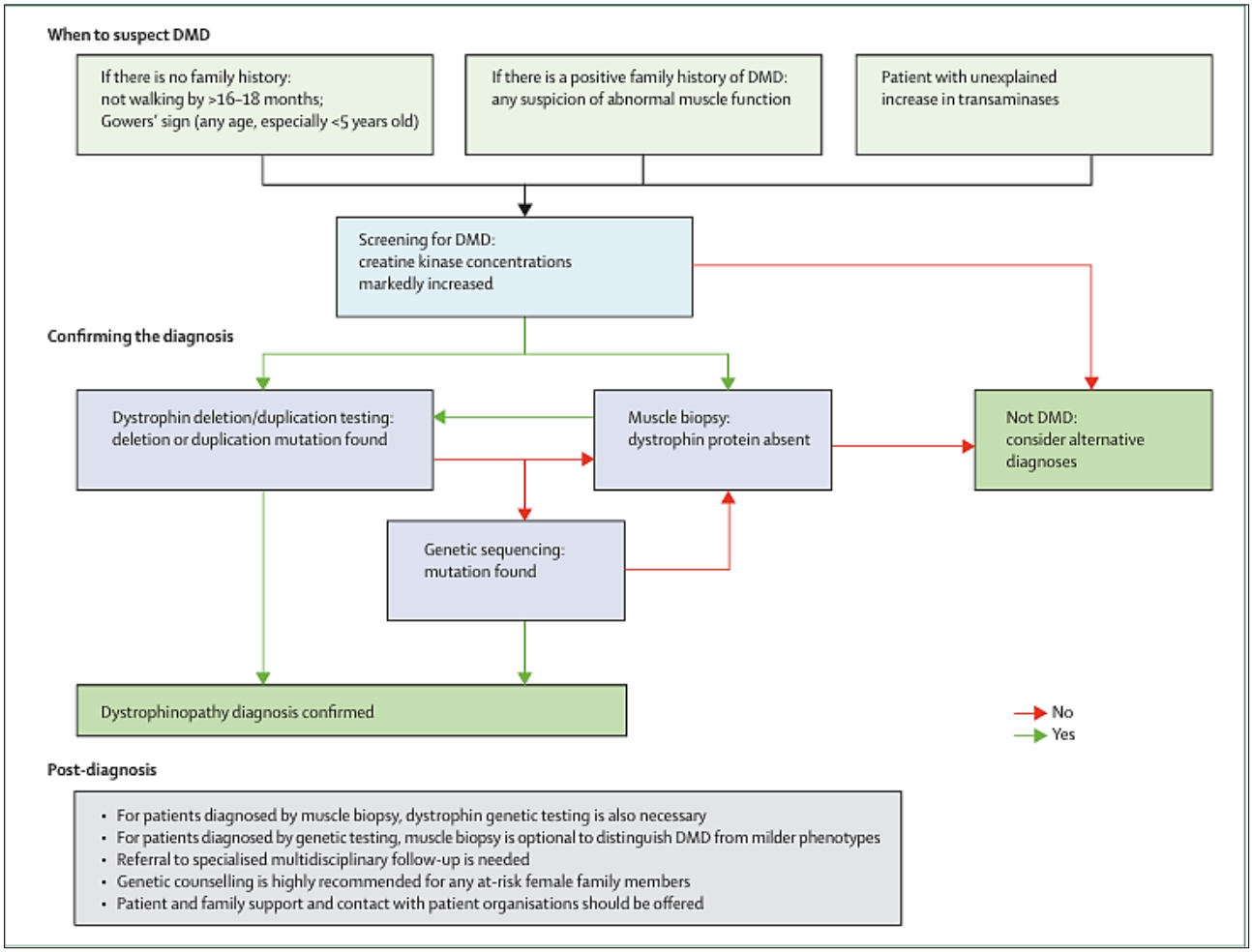


**Figure 4** Diagnosis of DMD: the pathway of the diagnosis to its confirmation (Thelancet.com. [cited 2025 Feb 25]. Available from: https://www.thelancet.com/pdfs/journals/laneur/PIIS1474-4422(09)70271-6.pdf)

*2.4.3. Biomarkers in muscular dystrophy*

Biomarkers are crucial for early detection and monitoring of disease progression and assessment of therapeutic efficacy in MD. Serum biomarkers, such as creatine kinase (CK) levels, are often elevated in patients with MD due to muscle cell breakdown and are useful for diagnosis, monitoring treatment response, and monitoring disease progression (Krebs *et al*., 2013; Mazzone *et al*., 2011). Recent research has identified novel biomarkers, including microRNAs, which are involved in regulating muscle cell processes and are altered in MD patients (Gonzalez *et al*., 2011), and circulating muscle-derived proteins, which may provide more precise insights into disease dynamics and therapeutic responses (Guglieri *et al*., 2023). Research into these biomarkers continues, intending to identify reliable indicators for early detection and disease monitoring.

## 3. Advancements in muscular dystrophy research

### 3.1. Molecular mechanisms and genetic insights

In the last ten years, there have been notable advancements in our understanding of the molecular mechanisms that contribute to muscle degeneration in muscular dystrophy (MD). A key achievement in MD research was identifying the dystrophin gene in the 1980s (Hoffman *et al*., 1987). Researchers have also discovered the importance of various proteins, such as utrophin—a protein similar to dystrophin—leading to innovative therapeutic approaches focused on boosting its expression to compensate for the deficiency of dystrophin (Wilmshurst *et al*., 2019). Furthermore, uncovering genetic mutations associated with other forms of MD, such as Limb-Girdle Dystrophy and Facioscapulohumeral Dystrophy, has opened up new possibilities for understanding and treating these conditions (Zatz & Kunkel, 2010). Recent research has also shed light on the roles of other proteins, including sarcoglycans and dystroglycans, in preserving muscle cell integrity. Investigations into the molecular processes behind muscle degeneration have also highlighted the contributions of oxidative stress, mitochondrial dysfunction, and inflammatory responses to the progression of MD (McDonald *et al*., 2013). These insights have led to new therapeutic targets and strategies to halt disease progression.

### 3.2. Gene therapy

Gene therapy for muscular dystrophy has advanced significantly, especially regarding Duchenne muscular dystrophy. Techniques for gene editing like CRISPR/Cas9 and exon skipping can directly alter the DMD gene to restore the expression of dystrophin (Goyenvalle *et al*., 2015). Utilizing CRISPR/Cas9 technology to fix mutations in the dystrophin gene presents considerable potential for permanently addressing the underlying genetic issues (Duan *et al*., 2017). Furthermore, exon skipping, which employs antisense oligonucleotides to bypass defective exons to correct the reading frame of the dystrophin gene, has shown encouraging results in clinical trials for DMD (Cirak *et al*., 2015), resulting in the approval of eteplirsen, the inaugural exon-skipping treatment for DMD (Cirak *et al*., 2011). Additional gene therapies aim to introduce functional versions of the dystrophin gene or utilize viral vectors to deliver therapeutic genes straight into muscle cells (Wilton *et al*., 2007).

### 3.3. Stem cell therapy

Stem cell therapies are being investigated as possible options for regenerating damaged muscle tissue in muscular dystrophy (MD). Recent research has concentrated on mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and myoblasts due to their capability to repair or replace injured muscle tissue and enhance regeneration. Although there are obstacles concerning immune rejection, the efficiency of engraftment, and limited functional recovery, stem cell therapies continue to be an important field of study (Xu *et al*., 2013; Goyenvalle *et al*., 2016) that has shown promise in improving muscle function in animal studies. However, difficulties persist in achieving durable engraftment and functional recovery in human cases (Krebs *et al*., 2013). The possibility of utilizing stem cells to mend damaged muscle tissue signifies an emerging area in the treatment of MD.

### 3.4. Regenerative medicine

Advances in regenerative medicine, including biomaterials and tissue engineering, show potential for muscle regeneration in muscular dystrophy (MD). Scaffolding materials combined with stem cells or growth factors aim to enhance tissue repair and reduce fibrosis, a key challenge in MD treatment (Sharma *et al*., 2019). Biocompatible scaffolds like collagen or hydrogels can be loaded with growth factors, such as IGF-1, to promote muscle cell proliferation and repair (Mann *et al*., 2014). Targeting molecular pathways involved in fibrosis, such as TGF-β signaling inhibition, has also shown promise in preclinical studies (Yoon *et al*., 2015). While the synergy of biomaterials and cell therapies is promising for improving muscle function in MD patients, challenges in delivery mechanisms, long-term survival, and tissue integration remain.

### 3.5. Molecular pathways and targeted drug therapies

Targeted drug therapies are being developed to tackle the complex molecular pathophysiology of muscular dystrophy (MD), focusing on key processes like inflammation, fibrosis, and muscle degeneration. These treatments include anti-inflammatory agents to reduce swelling and pain, antifibrotic drugs to limit scar tissue formation, and various molecules that promote muscle repair and regeneration. A notable example is corticosteroids, which effectively slow the progression of Duchenne muscular dystrophy (DMD), a severe form of MD (Passamano *et al*., 2012). Researchers are also exploring new drug candidates specifically targeting the molecular mechanisms of muscle regeneration, with these potential therapies currently in clinical trials (Miller *et al*., 2017). Overall, these advancements represent a promising direction in the fight against muscular dystrophy, offering hope for more effective treatments soon.

## 4. Therapeutic approaches in muscular dystrophy

### 4.1. Pharmacological treatments

Corticosteroids like prednisone and deflazacort are the primary pharmacological treatment for managing symptoms and slowing disease progression in muscular dystrophy (MD) patients. These medications enhance muscle strength, delay weakness, and prolong ambulation (McDonald *et al*., 2013). They reduce inflammation in muscle tissue; however, long-term use can result in side effects such as weight gain, osteoporosis, and growth retardation (Mazzone *et al*., 2011). Newer agents targeting muscle function, such as ezutromid, which boosts utrophin levels, are currently being studied (Guglieri *et al*., 2023). Additionally, drugs targeting fibrosis pathways, including TGF-β inhibitors, are under investigation to mitigate muscle fibrosis that impairs regeneration (Mendell *et al*., 2012). These treatments may be combined with other therapies to enhance long-term muscle function.

### 4.2. Gene-based therapies

Gene-based therapies, including exon skipping for MD and the use of antisense oligonucleotides (AONs) to restore the dystrophin reading frame, are among the most promising approaches in clinical research (Cirak *et al*., 2015). Several clinical trials have shown positive results with AONs, such as eteplirsen, the first FDA-approved exon-skipping drug approved for use in specific MD subgroups (Miller *et al*., 2017). These gene-based therapies represent a significant step toward personalized medicine for MD patients. Other RNA-based therapies, such as those targeting mRNA to restore protein expression or promote translational efficiency, are also being explored. These RNA-based strategies aim to address the root cause of the genetic mutations and offer long-term benefits by restoring muscle function and strength.

Additionally, gene therapies that introduce functional copies of the dystrophin gene or other related proteins into muscle cells through viral vectors have shown promise in preclinical and clinical trials (Wilton *et al*., 2007). However, challenges related to the delivery and integration of these therapies into muscle tissue, as well as the risk of immune reactions, remain areas of ongoing research.

### 4.3. Enzyme replacement therapy

Enzyme replacement therapy (ERT) treats specific metabolic forms of MD, notably Pompe disease, which arises from a deficiency of the enzyme acid α-glucosidase (GAA). This deficiency leads to glycogen accumulation in muscle cells, causing weakness and respiratory problems. ERT delivers recombinant GAA to break down glycogen, enhancing muscle function and delaying disease progression. While ERT has significantly improved outcomes for infants with early-onset Pompe disease, it presents challenges, including high costs and the necessity for lifelong treatment (Van der Beek *et al*., 2012). However, ERT is limited in conditions like Duchenne MD, where the root cause is a genetic mutation rather than an enzyme deficiency.

### 4.4. Surgical and physical therapy

Surgical and physical therapy interventions are crucial in managing muscular dystrophy (MD) alongside pharmacological treatments. Surgical procedures, such as orthopedic corrections for contractures and scoliosis, are vital in the advanced stages of MD to enhance mobility and quality of life. Physical therapy, combined with assistive devices like wheelchairs and braces, significantly improves patients' quality of life by focusing on the preservation of muscle strength, flexibility, and joint mobility (Rakowicz & Kennard, 2005). Early intervention in physical therapy is essential for optimizing functional outcomes, and tailored exercise programs have been effective in delaying muscle weakness and maintaining functional abilities (Mazzone *et al*., 2011).

## 5. Challenges in muscular dystrophy research and treatment

### 5.1. Genetic heterogeneity

A significant challenge in MD research and treatment is the genetic heterogeneity across the different subtypes of MD. MD encompasses a broad spectrum of disorders with a variety of genetic mutations, each with different effects on muscle function. Variations in the specific mutations within the same gene or in the genes associated with other MD subtypes lead to different disease manifestations, complicating both diagnosis and treatment (Zatz & Kunkel, 2010; Flanigan *et al*., 2014). This variability also makes personalized medicine approaches more complex.

### 5.2. Challenges in gene therapy delivery

Despite advances in gene editing and exon-skipping therapies, effectively and safely delivering these treatments to muscle tissue remains a major challenge. The use of viral vectors can provoke immune responses, which compromise their effectiveness and safety (Goyenvalle *et al*., 2015). Researchers are investigating new strategies to enhance delivery systems, including the creation of more efficient and targeted vectors (Duan *et al*., 2017). Furthermore, achieving widespread and lasting gene delivery to all affected muscle groups continues to be a significant obstacle. While efforts are underway to develop non-viral delivery systems and improve viral vectors, the need for precise and targeted delivery remains crucial.

### 5.3. Safety and efficacy of experimental therapies

The safety and efficacy of experimental therapies, such as gene editing, stem cell therapies, and molecular inhibitors for MD remain a critical concern. Although promising, many of these therapies are still in early-phase clinical trials, and long-term safety data are limited (Mendell *et al*., 2015). For example, gene therapies may inadvertently cause off-target genetic changes, and stem cell-based approaches may pose risks of immune rejection or tumor formation (Krebs *et al*., 2013). The regulatory approval process is stringent, and the complexity of designing clinical trials for rare diseases like MD presents additional obstacles.

### 5.4. Funding and resource allocation

As a rare disease, MD faces challenges in securing sufficient funding for research. Despite the growing interest in MD due to the advancements in gene therapy and molecular research, financial support for large-scale clinical trials, long-term studies, and global collaborations remains insufficient. Financial limitations restrict the scale of clinical trials and delay the development of new treatments, particularly in countries with limited healthcare resources. However, increased awareness and the involvement of advocacy organizations have led to more funding opportunities for research and therapeutic development (Tedesco & Cossu, 2012).

### 5.5. Long-term efficacy and monitoring

The long-term efficacy of MD therapies, especially gene and stem cell therapy, needs to be closely monitored to assess the durability of treatments and the overall impact on quality of life. Many clinical trials for MDs focus on short-term outcomes, such as muscle strength and mobility, but these measures may not fully capture the long-term impacts of treatments on patient quality of life. Additionally, since MD is a progressive disease, it can take years to assess the true effectiveness of a treatment, making long-term monitoring and follow-up essential (Mazzone *et al*., 2011). This requires rigorous long-term follow-up studies and a robust framework for evaluating patient outcomes to improve the precision and reliability of clinical trials. (Guglieri *et al*., 2023).

## 6. Future directions and emerging therapies

### 6.1. Crispr/cas9 and advanced gene editing

CRISPR/Cas9 has emerged as one of the most revolutionary tools for gene editing. This technique allows for precise genome modifications, offering the potential to correct mutations at the DNA level (Wakabayashi *et al*., 2021) a permanent solution for restoring functional proteins like dystrophin (Goyenvalle *et al*., 2015). While there are still challenges to overcome in terms of delivery and off-target effects, CRISPR/Cas9 holds enormous promise for the future of MD treatment (Dastgir *et al*., 2022). CRISPR/Cas9 allows for precise DNA editing at specific locations in the genome, which could eliminate or correct mutations responsible for MD.

### 6.2. Exosome-based therapies

Exosome-based therapies have emerged as a novel approach to gene delivery and tissue regeneration. Exosomes are nanoscale extracellular vesicles that can transfer genetic material, proteins, and other bioactive molecules between cells. These exosomes can act as natural delivery systems for therapeutic molecules, including RNA, proteins, and gene editing tools (Tominari *et al*., 2018). This makes them a promising candidate for treating genetic disorders like MD. Studies have shown that exosomes can be engineered to carry therapeutic genes or anti-inflammatory molecules, potentially facilitating muscle regeneration and repairing damaged tissues (Liu *et al*., 2020). Research into exosome-based drug delivery is still in its early stages regarding tissue regeneration in MD, with the advantage of minimal immune rejection and more precise targeting of affected muscle tissues. However, the technology holds promise for future therapeutic strategies in MD (Elsharkawy *et al*., 2020).

### 6.3. Personalized medicine

As our understanding of MD genetics and the variability in disease progression increases, personalized medicine is becoming a central focus for treatment strategies. Tailoring therapies based on the individual's specific genetic profile and disease characteristics can lead to more effective and targeted treatments. This may involve selecting the most appropriate gene therapy or drug treatments based on a patient's specific mutation or subtype of MD. Precision medicine is particularly relevant in MD, given the heterogeneity of genetic mutations and their variable phenotypic expressions (Brouwer *et al*., 2021). Personalized approaches are also anticipated to improve the safety and efficacy of new treatments, especially gene therapy and RNA-based therapies, thus improving treatment outcomes and reducing the risk of side effects (Flanigan *et al*., 2014).

### 6.4. Nanotechnology and drug delivery systems

Nanotechnology presents groundbreaking opportunities for enhancing drug delivery systems in muscular dystrophy (MD), particularly by addressing the significant challenge of ensuring that therapeutic agents reach muscle tissues directly. By utilizing nanoparticles and nanocarriers, researchers can devise methods to effectively encapsulate various drugs and genetic materials, thereby facilitating targeted and controlled release specifically at sites experiencing muscle degeneration. This novel approach not only helps minimize potential side effects commonly associated with systemic drug delivery but also improves the overall therapeutic efficacy of the administered drugs. Recent studies have indicated that various nanoparticle-based systems, including liposomes, polymeric nanoparticles, and micelles, have been rigorously investigated for their ability to enhance the delivery of RNA-based therapeutics and anti-inflammatory agents as part of MD treatment strategies. Such advancements in nanotechnology could pave the way for more effective therapies, potentially transforming the treatment landscape for individuals affected by muscular dystrophy, making it a promising area of research and clinical application (Rahimian *et al*., 2020; Boronat *et al*., 2020; Ebrahimi *et al*., 2022).

## 7. Conclusion

### *Summary of key findings*

Recent advancements in muscular dystrophy research have provided valuable insights into the genetic and molecular mechanisms that contribute to muscle degeneration. Promising therapeutic strategies, such as gene therapy, stem cell therapy, and regenerative medicine, have emerged to help slow disease progression, restore muscle function, and enhance patients' quality of life. Improvements in genetic testing, imaging techniques, and the identification of new biomarkers have strengthened diagnostic capabilities. While there are still challenges—particularly related to genetic diversity, delivery systems, and long-term safety and efficacy—the field has made notable progress in enhancing the quality of life for individuals with muscular dystrophy.

### *Outlook for the future*

The future of MD therapy is promising, with emerging technologies such as CRISPR/Cas9, exosome-based therapies, nanotechnology, and personalized medicine providing new avenues for treatment. However, challenges such as the complexity of genetic mutations, the need for targeted delivery systems, and the long-term monitoring of experimental therapies must be addressed before these treatments become widely available. The hope is that future breakthroughs will not only improve the lifespan and mobility of individuals with MD but also offer potential cures for some forms of the disease.

### *Call for continued research and collaboration*

The continued success of MD research will require interdisciplinary collaboration between geneticists, molecular biologists, clinicians, and pharmaceutical companies. It is essential to foster a global network of researchers and healthcare professionals who can share data, experiences, and resources to advance the development of effective treatments. Multinational collaborations will accelerate the pace of discovery and clinical trial recruitment, especially for rare forms of MD.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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