Τελευταίες εξελίξεις στις κλινικές μελέτες για την αντιμετώπιση της Μυικής Δυστροφίας Duchenne(DMD) και η σημασία της έγκαιρης διάγνωσης και αντιμετώπισης

Μούντης Αλέξανδρος
Χειρούργος Οδοντίατρος ΑΠΘ,

Εκπρόσωπος Ομάδας Γονέων Β. Ελλάδος MDA Hellas (Parent Project MDA HELLAS)

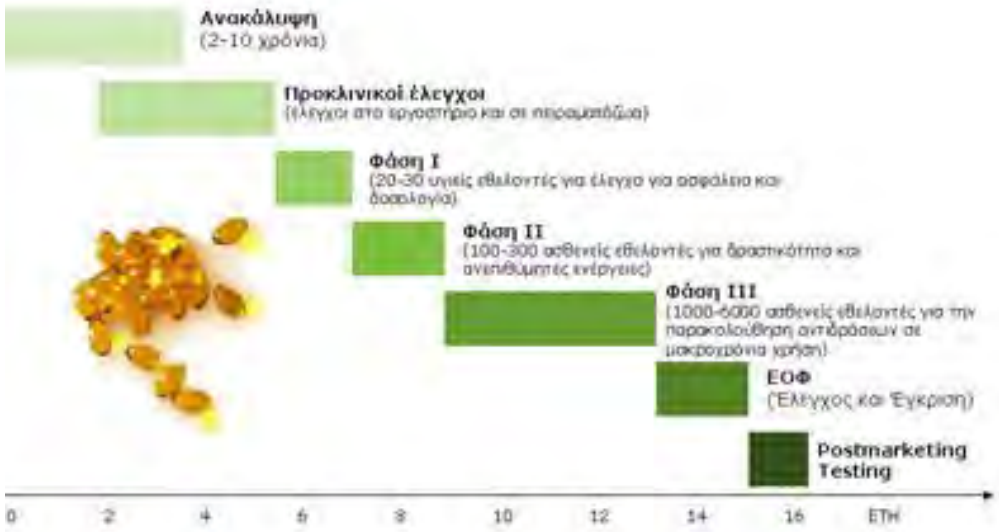
Μέλος Οδοντιατρικής Ακαδημίας
Μέλος ΣΕΒΕ και ΟΣΘ

MDA ΕΛΛΑΣ
ΣΩΜΑΤΕΙΟ ΦΡΟΝΤΙΔΑΣ ΑΤΟΜΩΝ ΜΕ ΝΕΥΡΟΜΥΪΚΕΣ ΠΑΘΗΣΕΙΣ

United Parent Projects Muscular Dystrophy

Ευρευνητικές Στατηγικές για την αντιμετώπηση του DMD

- Gene Therapy
- Cell Therapy
- Pharmacological Therapies
- Utrophin Upregulators
- Myostatin Inhibitors
- Exon-skipping



Τελευταίες εξελίξεις στις κλινικές μελέτες Phase II/III/IV

TRANSLARNA (Ataluren) - A New Drug for Nonsense Mutations by PTC Therapeutics Phase IV

CATENA®/RAXONE® - Study of Idebenone in Duchenne (DELOS) Phase III
TADALAFIL - Trial of Tadalafil for Duchenne Phase III
SPIRONOLACTONE and EPLERENONE - Therapeutic Potential for Aldosterone Inhibition in Duchenne Phase III

ETEPLIRSEN - Exon skipping Using Phosphorodiamidate Morpholino Oligomers (PMO) to produce functional dystrophin protein Sarepta
ETEPLIRSEN - Study 4658-203 for Early Stage Duchenne
ETEPLIRSEN - Study 4658-204 for Advanced Stage Duchenne

VBP15 - A Novel Steroid Customized for Duchenne Phase II
SMT C1100 - A Small Molecule Utrophin Modulator for Duchenne Phase II
PF-06252616 - Pfizer's Myostatin Inhibitor Phase II
CAT-1004 - Catabasis' MoveDMD Trial Phase II
ISOFEN 3 - A combination drug for the treatment of Duchenne Phase II
PF-06252616 - Pfizer's Myostatin Inhibitor Phase II

Τελευταίες εξελίξεις στις κλινικές μελέτες Phase I/II

BMS-986089 - Bristol-Myers Squibb's Candidate for Myostatin Inhibition Phase 1/2

FOLLISTATIN GENE TRANSFER - Clinical Intramuscular Gene Transfer of rAAV1.CMV.huFollistatin344 Trial to Patients With Duchenne Phase 1/2

MYOBLAST TRANSPLANTATION - Myoblast Transplantation in Duchenne Patients Phase 1/2

DT-200 - A Selective Androgen Receptor Modulator to Improve Muscle Strength & Function in Duchenne Phase I

GALGT2 Gene Therapy - Viral gene transfer for GALGT2 as a surrogate gene therapy for Duchenne Phase I

GENE TRANSFER OF MICRO-DYSTROPHIN - Clinical Intramuscular Gene Transfer Trial of rAAVrh74.MCK.Micro-Dystrophin Phase I

Τελευταίες εξελίξεις στις κλινικές μελέτες Preclinical

TAMOXIFEN - Using tamoxifen to improve muscle strength in DMD/BMD

LAMININ-111 - Laminin-111, Integrin and Utrophin as a Potential Therapy for DMD

RTC13 Read-Through Compound - Development of a drug that corrects nonsense mutations in patients with Duchenne

COENZYME Q10 AND LISINOPRIL - Clinical Trial of Coenzyme Q10 and Lisinopril in Muscular Dystrophies

ARM210 - Using ARM210 to Improve Muscle Strength & Function in DMD

NBD Peptide - Using NF-κB blockers to Decrease Inflammation and Improve Muscle Function in Duchenne

LAMININ-111 - Laminin-111, Integrin and Utrophin as a Potential Therapy for Duchenne

iPS CELL THERAPY - Induced Pluripotent Stem Cells for Duchenne

Τελευταίες εξελίξεις στις κλινικές μελέτες Preclinical

BIGLYCAN - A Unique Utrophin Upregulator

CARMESEAL-MD - Poloxamer 188 N

AT-300 - Akashi's Novel Modulator of Stretch-Activated Calcium Channels

DT-200 - A Selective Androgen Receptor Modulator to Improve Muscle Strength & Function in Duchenne

EXON 2 SKIPPING - To induce Internal Ribosomal Entry Site (IRES) activation in Duchenne patients with Exon 2 Duplications

HT-100 - Akashi's Phase 1/2 Clinical Program in Duchenne – Stopped

DEFLAZACORT - A Pharmacokinetic Study of Oral Deflazacort in Children and Adolescents with Duchenne

STEROIDS IN YOUNG BOYS - Historically Controlled Trial of Corticosteroids in Young Boys With Duchenne

Τελευταίες εξελίξεις στις κλινικές μελέτες Preclinical

FOR-DMD - Finding the Optimal steroid Regimen for Duchenne Muscular Dystrophy
ImagingDMD - Magnetic Resonance Imaging and Biomarkers for Muscular Dystrophy
MICROSOFT BAND - A Potential Outcome Measure for Boys with Duchenne
MRI and CARDIOPULMONARY FUNCTION - Using MRI to Assess Cardiopulmonary Function in Duchenne
DP ARF ULTRASOUND - Double Push Acoustic Radiation Force Ultrasound for Monitoring Degeneration
STRENGTH TRAINING - Development of a Strength Training Protocol in Duchenne
COUGH in DUCHENNE and BECKER - Peak Cough Flow and Cough Clearance in Duchenne and Becker Muscular Dystrophy
BECKER MUSCULAR DYSTROPHY - A Natural History Study to Predict Efficacy of Exon Skipping
DUCHENNE MUSCULAR DYSTROPHY - A Longitudinal Study of the Natural History of Duchenne

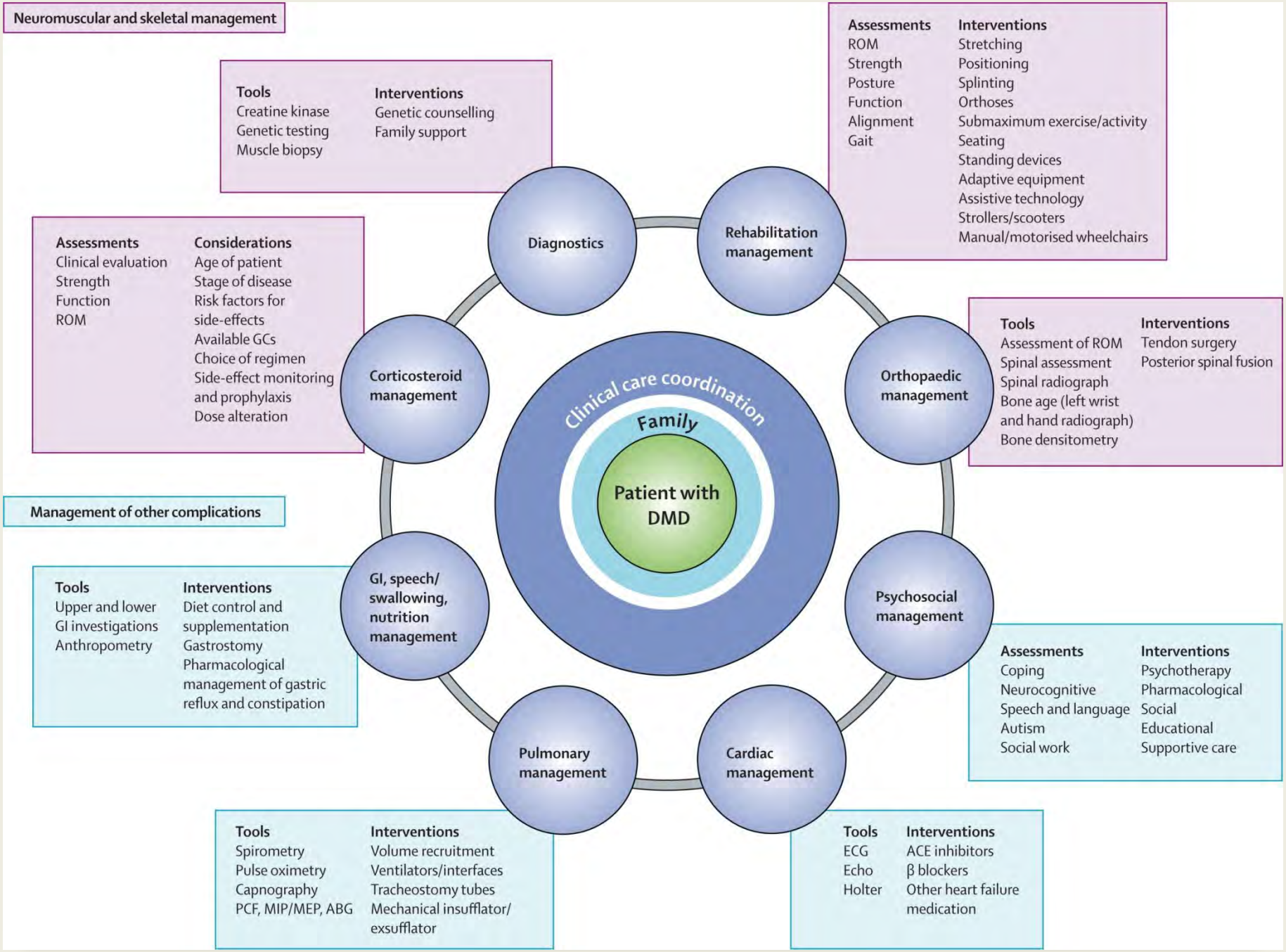
http://www.parentprojectmd.org/site/PageServer?pagename=Advance_pipeline

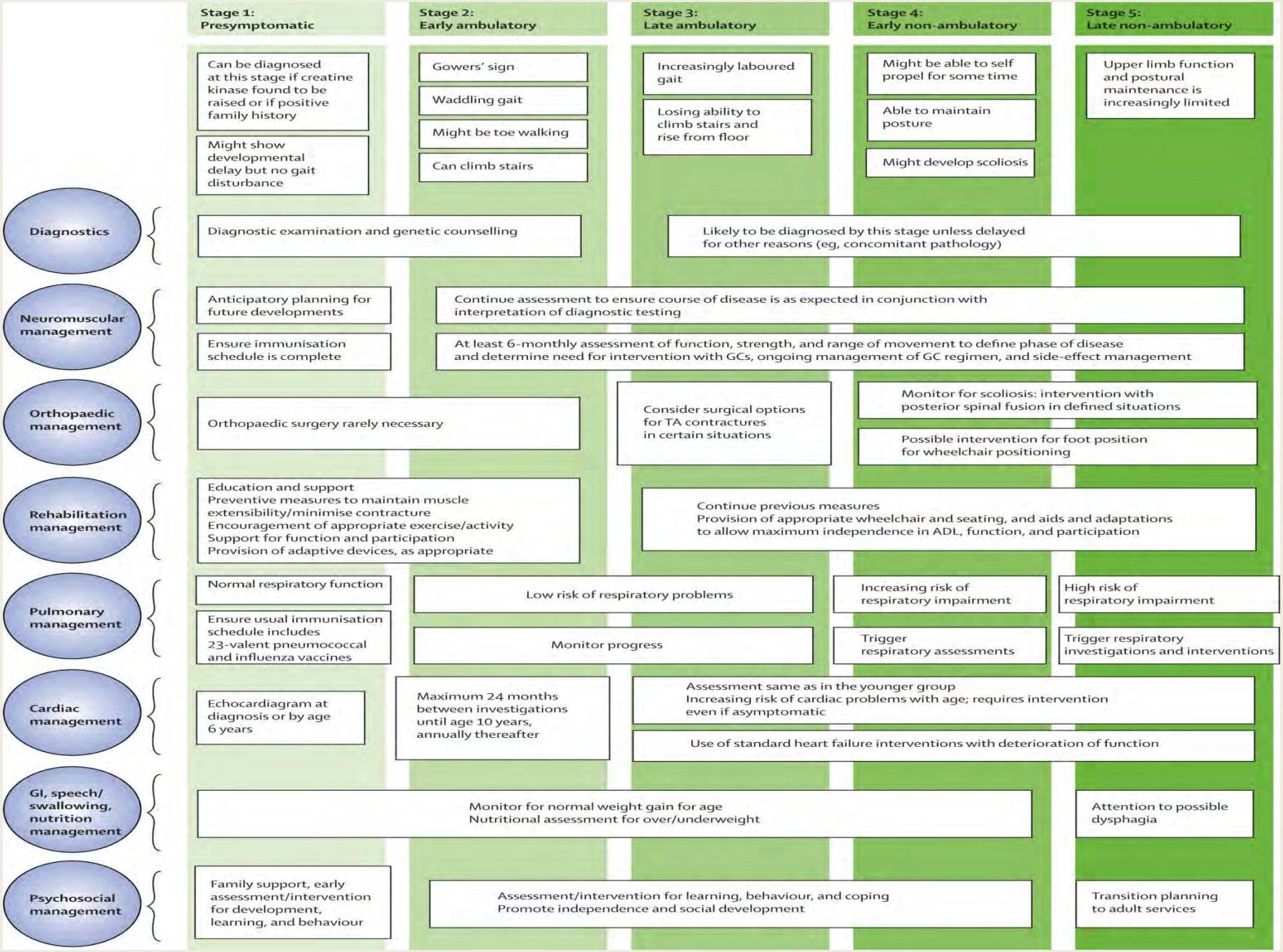
Η σημασία της έγκαιρης διάγνωσης και αντιμετώπισης [1]

- Γενετική συμβουλευτική
- Έγκαιρη Φυσιοθεραπευτική υποστήριξη
- Έγκαιρη παρέμβαση με λογοθεραπεία και εργοθεραπεία
- Έγκαιρη φαρμακευτική υποστήριξη για την προστασία του μυικού ιστού και των οστών
- Διατροφολογική συμβουλευτική και συμπληρώματα διατροφής
- Προστασία από την χρήση μη κατάλληλων φαρμάκων (πχ αναισθησίας [2])
- Προστασία του μυικού ιστού από ακατάλληλες δραστηριότητες
- Οικογενειακός προγραμματισμός

Ref.

1. Bushby K, Finkel R, Birnkrant DJ *et al*DMD Care Considerations Working Group: Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *Lancet Neurol* 2010; **9**: 77–93.
2. Breucking E, Reimnitz P, Schara U, Mortier W. Anesthetic complications. The incidence of severe anesthetic complications in patients and families with progressive muscular dystrophy of the Duchenne and Becker types. Anaesthetist 2000; 49: 187-195


Neuromuscular and skeletal management
Tools
Creatine kinase
Genetic testing
Muscle biopsy
Interventions
Genetic counselling
Family support
Assessments
ROM
Strength
Posture
Function
Alignment
Gait
Interventions
Stretching
Positioning
Splinting
Orthoses
Submaximum exercise/activity
Seating
Standing devices
Adaptive equipment
Assistive technology
Strollers/scooters
Manual/motorised wheelchairs
Assessments
Clinical evaluation
Strength
Function
ROM
Considerations
Age of patient
Stage of disease
Risk factors for side-effects
Available GCs
Choice of regimen
Side-effect monitoring and prophylaxis
Dose alteration
Diagnostics
Rehabilitation management
Corticosteroid management
Orthopaedic management
Clinical care coordination
Family
Patient with DMD
Tools
Assessment of ROM
Spinal assessment
Spinal radiograph
Bone age (left wrist and hand radiograph)
Bone densitometry
Interventions
Tendon surgery
Posterior spinal fusion
Management of other complications
Tools
Upper and lower GI investigations
Anthropometry
Interventions
Diet control and supplementation
Gastrostomy
Pharmacological management of gastric reflux and constipation
GI, speech/ swallowing, nutrition management
Psychosocial management
Assessments
Coping
Neurocognitive
Speech and language
Autism
Social work
Interventions
Psychotherapy
Pharmacological
Social
Educational
Supportive care
Pulmonary management
Cardiac management
Tools
Spirometry
Pulse oximetry
Capnography
PCF, MIP/MEP, ABG
Interventions
Volume recruitment
Ventilators/interfaces
Tracheostomy tubes
Mechanical insufflator/ exsufflator
Tools
ECG
Echo
Holter
Interventions
ACE inhibitors
β blockers
Other heart failure medication


Stage 1: Presymptomatic
Stage 2: Early ambulatory
Stage 3: Late ambulatory
Stage 4: Early non-ambulatory
Stage 5: Late non-ambulatory
Can be diagnosed at this stage if creatine kinase found to be raised or if positive family history
Might show developmental delay but no gait disturbance
Gowers' sign
Waddling gait
Might be toe walking
Can climb stairs
Increasingly laboured gait
Losing ability to climb stairs and rise from floor
Might be able to self propel for some time
Able to maintain posture
Might develop scoliosis
Upper limb function and postural maintenance is increasingly limited
Diagnostics
Diagnostic examination and genetic counselling
Likely to be diagnosed by this stage unless delayed for other reasons (eg, concomitant pathology)
Neuromuscular management
Anticipatory planning for future developments
Ensure immunisation schedule is complete
Continue assessment to ensure course of disease is as expected in conjunction with interpretation of diagnostic testing
At least 6-monthly assessment of function, strength, and range of movement to define phase of disease and determine need for intervention with GCs, ongoing management of GC regimen, and side-effect management
Orthopaedic management
Orthopaedic surgery rarely necessary
Consider surgical options for TA contractures in certain situations
Monitor for scoliosis: intervention with posterior spinal fusion in defined situations
Possible intervention for foot position for wheelchair positioning
Rehabilitation management
Education and support
Preventive measures to maintain muscle extensibility/minimise contracture
Encouragement of appropriate exercise/activity
Support for function and participation
Provision of adaptive devices, as appropriate
Continue previous measures
Provision of appropriate wheelchair and seating, and aids and adaptations to allow maximum independence in ADL, function, and participation
Pulmonary management
Normal respiratory function
Ensure usual immunisation schedule includes 23-valent pneumococcal and influenza vaccines
Low risk of respiratory problems
Monitor progress
Increasing risk of respiratory impairment
Trigger respiratory assessments
High risk of respiratory impairment
Trigger respiratory investigations and interventions
Cardiac management
Echocardiagram at diagnosis or by age 6 years
Maximum 24 months between investigations until age 10 years, annually thereafter
Assessment same as in the younger group
Increasing risk of cardiac problems with age; requires intervention even if asymptomatic
Use of standard heart failure interventions with deterioration of function
GI, speech/ swallowing, nutrition management
Monitor for normal weight gain for age
Nutritional assessment for over/underweight
Attention to possible dysphagia
Psychosocial management
Family support, early assessment/intervention for development, learning, and behaviour
Assessment/intervention for learning, behaviour, and coping
Promote independence and social development
Transition planning to adult services

ΕΥΧΑΡΙΣΤΩ

Ομάδα Γονέων Β. Ελλάδος MDA Hellas
(Parent Project MDA HELLAS)

MDA ΕΛΛΑΣ
ΣΩΜΑΤΕΙΟ ΦΡΟΝΤΙΔΑΣ ΑΤΟΜΩΝ ΜΕ ΝΕΥΡΟΜΥΪΚΕΣ ΠΑΘΗΣΕΙΣ

United Parent Projects
Muscular Dystrophy