Newborn Screening ACT Sheet

[Elevated creatine kinase muscle isoform (CK-MM)]
Genetic Neuromuscular Disease

Differential Diagnosis: Duchenne Muscular Dystrophy (DMD), Becker Muscular Dystrophy (BMD), DMD-associated dilated cardiomyopathy (DMD associated-DCM), and other neuromuscular disorders.

Condition Description: Highly elevated levels of the muscle isoform of creatine kinase (CK-MM) are associated with neuromuscular diseases. Most elevations will be associated with DMD and BMD. These are degenerative neuromuscular diseases caused by a defect in the dystrophin (*DMD*) gene. DMD and BMD have similar signs and symptoms but are considered to be the same underlying disease that differs in age of onset and severity. DMD/BMD is an X-linked recessive disorder that primarily affects males although females may be affected. Dystrophinopathies occur in approximately 1 in 5,000 males. There are other genetic neuromuscular conditions that may also explain highly elevated CK-MM, with variable modes of inheritance.

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact family to inform them of the newborn screening result and ascertain clinical status.
- Provide the family with basic information about risk for DMD/BMD and other neuromuscular disorders.
- Elicit family history of signs and symptoms of neuromuscular disease.
- Consult with the neuromuscular disease specialist or comprehensive MDA clinic.
- Refer for genetic counseling.
- Report findings to state newborn screening program.

Diagnostic Evaluation: After confirmation of the CK-MM elevation, molecular genetic testing of the *DMD* gene can establish the diagnosis. If positive for a pathogenic variant in the *DMD* gene, additional evaluation may include cardiac, neurological, and neuromuscular testing. If negative, molecular testing of a broader neuromuscular disease gene panel may suggest other etiologies. Some of the conditions associated with those genes (e.g., *Pompe disease*, spinal muscular atrophy) may already be screened by other methods since they are on the Recommended Uniform Screening Panel (RUSP).

Clinical Considerations: CK-MM elevations are associated with diseases of variable severity and age of onset of which DMD/BMD is the most common. Subtle signs and symptoms may appear between the first and second years of life, specifically proximal leg weakness. Gene therapies may be available and additional therapies are being developed. Ongoing multi-specialty care is necessary.

Additional Information:
Gene Reviews
Genetics Home
OMIM

Referral (local, state, regional and national):
Testing
Find Genetic Service
Muscular Dystrophy Association Clinics
PPMD Certified Duchenne Care Centers Network
ClinicalTrials.gov

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Translating Genes Into Health®

LOCAL RESOURCES: Insert State newborn screening program web site links

State Resource site *(insert state newborn screening program website information)*

Name	
URL	
Comments	

Local Resource Site *(insert local and regional newborn screening website information)*

Name	
URL	
Comments	

APPENDIX: Resources with Full URL Addresses

Additional Information:

Gene Reviews
https://www.ncbi.nlm.nih.gov/books/NBK1119/

Genetics Home Reference
https://ghr.nlm.nih.gov/gene/DMD

OMIM
https://www.omim.org/entry/310200

Referral (local, state, regional and national):

Testing
https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=DMD

Find Genetic Services
https://clinics.acmg.net

Muscular Dystrophy Association Clinics
https://www.mda.org/care/mda-care-centers

PPMD Certified Duchenne Care Centers Network
https://www.parentprojectmd.org/care/find-a-certified-duchenne-care-center/

ClinicalTrials.gov
https://clinicaltrials.gov/

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