

Acute Flaccid Myelitis Task Force - Update -

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**CDC Board of Scientific Counselors, Office of Infectious Diseases
Atlanta, GA**

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AFM Task Force - Terms of Reference

Present findings, observations, and outcomes to CDC Board of Scientific Counselors (BSC), Office of Infectious Diseases for discussion, deliberation, and decision

- Etiologies and pathogenesis
 - Evaluate current understanding and the pathogenic mechanisms of AFM
 - Review available data and develop hypotheses about possible or likely etiologies and the pathogenesis of AFM
 - Propose new studies, study designs, laboratory techniques, assays, and other activities to address specific hypotheses on AFM etiologies and pathogenesis
 - Develop and prioritize findings and observations for the BSC to utilize in the development of recommendations for areas of further study or investigation
- Clinical treatment
 - Build on existing information on clinical practices by seeking information on clinical experience with the treatment of AFM
 - Identify research gaps in the diagnosis and treatment of AFM
 - Develop potential findings and observations on patient management for referral to the BSC

AFM Task Force Membership

- **BSC Members**

- Emily Erbeling, National Institutes of Health Div. of Microbiology & Infectious Diseases (*Ex Officio*)
- Ruth Lynfield, Minnesota Dept. of Health
- Bonnie Maldonado, Stanford University School of Medicine, Depts. of Pediatrics and Health Research and Policy
- Jill Taylor, New York State Dept. of Health, Wadsworth Laboratory
- Kevin Messacar, University of Colorado School of Medicine Dept. of Pediatrics
- John Modlin, Bill & Melinda Gates Foundation, Polio Research and Policy
- Nancy Murphy, University of Utah, Dept. of Pediatrics and Physical Medicine & Rehabilitation
- Avi Nath, National Institutes of Health, National Institute of Neurological Disorders and Stroke

- **AFM Clinical and Research Experts**

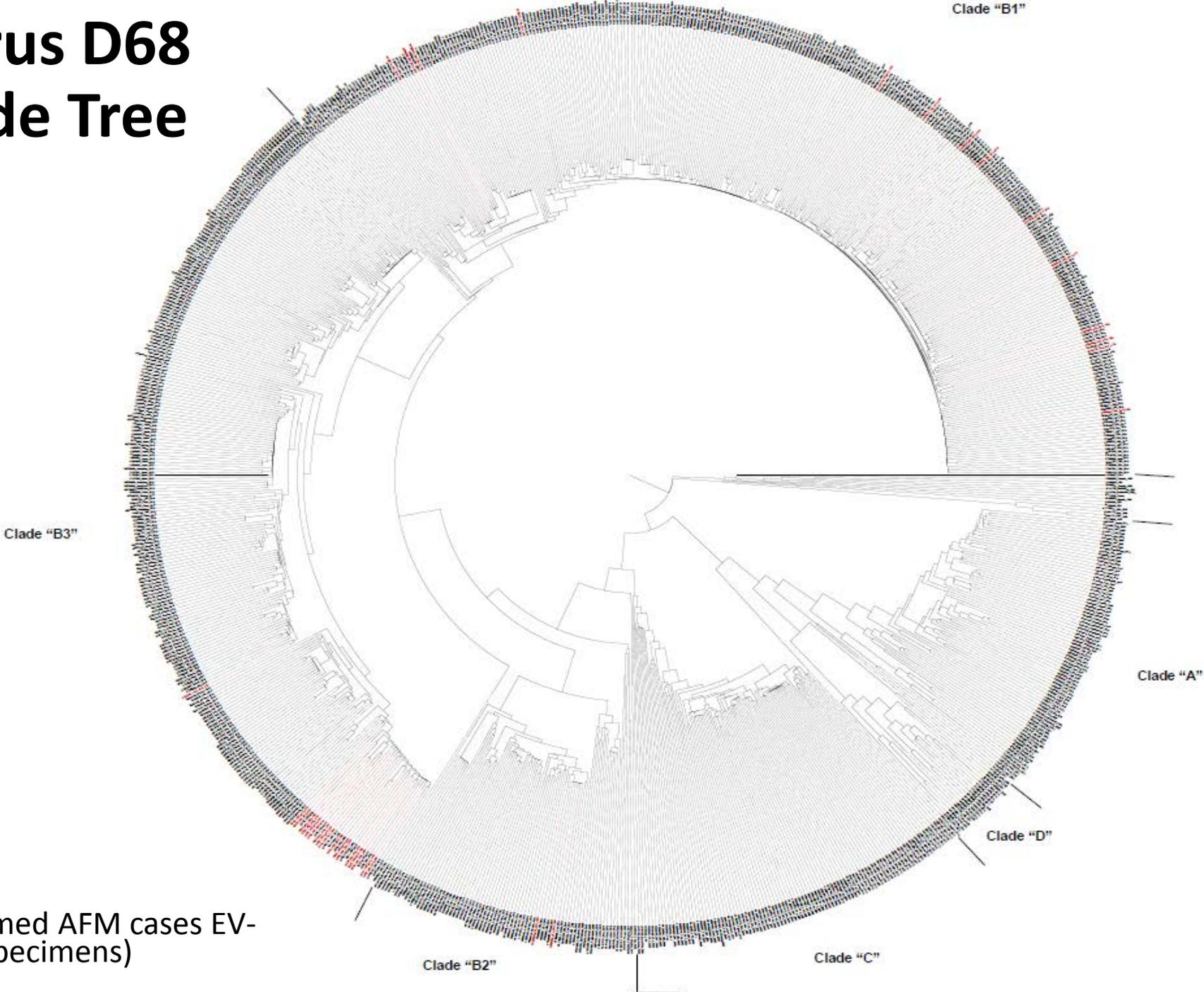
- Leslie Benson, Boston Children's Hospital, Dept. of Neurology
- Benjamin Greenberg, University of Texas Southwestern Medical Center, Dept. of Neurology and Neurotherapeutics
- Bryan Grenfell, Princeton University, Ecology and Evolutionary Biology and Public Affairs, Woodrow Wilson School
- Tory Johnson, Johns Hopkins University School of Medicine, Dept. of Neurology
- Carlos Pardo-Villamizar, Johns Hopkins University School of Medicine, Dept. of Neurology, Johns Hopkins Transverse Myelitis Center
- Matthew Schniederjan, Emory University School of Medicine, Dept. of Pathology
- Nate Smith, Arkansas Dept. of Health
- Ken Tyler, University of Colorado School of Medicine Chair, Dept. of Neurology
- Arun Venkatesan, Johns Hopkins University School of Medicine, Div. and Physical Med of Neuroimmunology and Neuroinfectious Diseases

AFM Task Force – Activities Since December 2018

BSC Meeting

- January-March 2019: monthly conference calls
 - Form AFM collaboration to
 - Strengthen infrastructure for case identification and surveillance, including long-term follow-up of cases
 - Facilitate research evaluations through case identification, data and specimen collection, and information sharing
 - Immunology: approaches to determine if pathology is due to direct effect of virus or damage due to immune response to virus
 - Host genetics and AFM
- April 2019: in-person meeting
 - Reviewed ongoing research projects and other activities
 - Prioritized virology and immunology research questions
 - Defined key knowledge gaps in genetics and treatment, including rehabilitation
 - Updated Task Force on the AFM natural history study (NIH)

Enterovirus D68 Nucleotide Tree



In red: CDC confirmed AFM cases EV-D68 (respiratory specimens)

Continuum of AFM Pathogenesis-related Research Questions



AFM Task Force – Process for Prioritization of Virology and Immunology Research Questions

- Before the in-person meeting
 - TF members submitted research questions to address the gaps on AFM etiology and pathogenesis
 - Two TF subgroups (TF members with immunology and virology expertise) discussed and categorized the questions by subtopics/buckets; performed a pre-meeting prioritization
- In-person meeting
 - Research questions discussed at length by category
 - Session on integration of research questions, including non-virology and immunology questions (putting it all together)
 - TF members individually prioritized the questions on the integrated categories; responses compiled

AFM Task Force – Main Categories for Action and Research

- Communication and education
- Surveillance
- Diagnostic tool development
- Pathogenesis
- Risk factors studies
- Therapeutics and vaccines
- Treatment and rehabilitation

AFM Task Force – High Priority Activities by Category

Category	Priority Activities
Communication & education	<ul style="list-style-type: none">• Communication and education efforts targeting health care providers, parents, and general public
Surveillance	<ul style="list-style-type: none">• Robust, integrated case and viral surveillance• Understand molecular epidemiology of EV-D68 strains• Investigate temporal and geographic correlations of AFM cases with circulating viruses
Diagnostic tool development	<ul style="list-style-type: none">• Detection of pathogen, host immune response• Develop immunologic assays (e.g., EV-D68 IgM) in CSF and serum• Detect exposure to infectious agents via the intrathecal antibody profile of AFM patients
Pathogenesis	<ul style="list-style-type: none">• Determine viral molecular determinants of neurotropism, cell death, paralytic potential• Use animal models to better understand viral pathogenesis• Determine if there is evidence of autoimmunity• Develop EV-D68 infectious clones

AFM Task Force – High Priority Activities by Category (cont.)

Category	Priority Activities
Risk factor studies	<ul style="list-style-type: none">• Epidemiologic risk factor studies• Determine genetic determinants of risk involved in immune regulation that may contribute to disease susceptibility or severity
Therapeutics & vaccines	<ul style="list-style-type: none">• Consider pre-clinical vaccine candidate development work
Treatment & rehabilitation	<ul style="list-style-type: none">• Standardize outcome measures (strength, QoL, community participation)• Long term follow-up of AFM patients

AFM Task Force – Key Findings

- Etiologies and pathogenesis
 - Non-polio enteroviruses, and EV-D68 in particular, are leading candidates for AFM etiology; other etiologies should continue to be examined
 - Would be helpful to develop additional diagnostic assays
 - Kinetics of disease suggests direct infection of spinal cord more likely than antibody-mediated pathology
 - Suggestions for further investigation into pathogenesis
- Clinical treatment
 - Need for standardized outcome measures (including for rehabilitation)
 - Treatment and rehabilitation may need to be individualized for each patient
 - Interim: establish a network of centers of expertise around the country to act as a resource for clinicians
- Suggestion for federal inter-agency AFM group to facilitate communication and enhance complementary approaches

Questions for BSC

- Do you agree with the main categories for action/research?
- Do you agree with the high priorities?
- Any other high priority areas for consideration?
- Suggestions for ways to ensure that clinicians recognize AFM and report to their health department?
- Other recommendations?

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