AFM Taskforce

Co-Chairs: Ruth Lynfield and Jill Taylor

AFM Taskforce Membership

- **BSC Members:**
  - Emily Erbelding, National Institutes of Health, Division of Microbiology and 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
- **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
  - Kevin Messacar, Children's Hospital Colorado, Pediatric Infectious Diseases
  - John Modlin, Bill & Melinda Gates Foundation, Polio
  - Avi Nath, National Institutes of Health, National Institute of Neurological Disorders and Stroke
  - Carlos Pardo-Vallamizar, Johns Hopkins University School of Medicine, Depts. Of Pathology and Neurology
  - Matthew Schniederjan, Emory University School of Medicine, Neuropathology
  - Nate Smith, Director and State Health Officer, Arkansas Department of Health
  - Ken Tyler, University of Colorado School of Medicine, Dept. of Neurology
  - Arun Venkatesan, Johns Hopkins University School of Medicine, Div. of Neuroimmunology and Neuroinfectious Diseases

Parents' Perspectives

- Jeremy Wilcox
- Rachel Scott
- Robin Roberts

Neurologic/Clinical Session

- Support for the emergence of novel AFM epidemiology in 2014
  - Rapidity of paralysis, epidemiologic pattern of cases and degree of cervical involvement distinguish AFM from other paralytic diseases like transverse myelitis
  - Striking biennial, seasonal peaks
  - Sporadic cases may have occurred previously, and received other diagnoses
- Support for use of sensitive clinical criteria (acute flaccid weakness) for surveillance purposes
  - Subsequent analysis of sub-populations
    - Sensitive definition will further characterize spectrum of illness
    - Specific definition will inform research questions around etiology and pathogenesis

Neurologic/Clinical (cont.)

- Understanding MRI lesions can help inform pathogenesis
  - The timing of the MRI critical to interpretation of findings
  - In patients with only cervical cord affected by MRI, lower extremity weakness due to white matter involvement
  - Important to consider treatment modalities for both grey and white matter disease within the cord
- Support for rigorous and standardized long term follow-up with strength and functional assessments
- Recognize that analysis of treatment outcomes exceedingly difficult with small patient pool and lack of standardized measurements across institutions

Virology & Pathogen Discovery

- Support for link between preceding virus-like illness and AFM
- EV-D68 remains the leading hypothesis for virus trigger despite other EV/RV detections and majority of respiratory specimens negative
- Support for understanding duration of shedding to interpret respiratory specimen results and timing of specimen collection
- Support for improved understanding of enterovirus epidemiology (temporal and geographic) in the US with focus on respiratory disease
- The failure to consistently detect a pathogen in the CSF is likely to remain true even with the planned enhanced discovery methods

Host Immune Response and Immune-mediated Pathogenesis

- Support for measuring antibody response to infection in serum and CSF
  - Diagnostic (intrathecal), pathogenic antibodies (autoantibodies)
  - Antibody-dependent enhancement
- Support for broad approaches to measuring pathogen-specific responses
  - Multi-pathogen peptide microarrays
  - Immune cell receptor repertoire profiling
- Support for measuring and characterizing EV-D68 population immunity
- Kinetics of disease suggest that antibody-mediated pathology is unlikely
  - Low priority given to measuring autoantibody responses

Host Risk Factors

- General support for assessing genetic risk factors associated with AFM
- Recognition that host genetics studies can be complex and expensive
- Target specific gene subsets
  - Central nervous system, immune system
  - Factors that influence tissue susceptibility: receptor polymorphisms
- Support for detailed, structured interviews with families to uncover other potential risk factors
  - Environmental, behavioral

Themes That Came Out of the AFM-TF Meeting

- Important to have strong collaboration encompassing CDC, NIH, expert academic partners and health departments
- Need for understanding CNS damage: direct pathogen effects, immune response
    - Non-human primate model and other model systems may be useful
- Continue work on pathogen detection
- Review and summarize clinical phenotypes of cases

Themes That Came Out of the AFM-TF Meeting (cont.)

- Strengthen case identification and surveillance
  - Work with partners to optimize recognition of AFM
  - Utilize surveillance for risk factor and other studies
- Strengthen and expand education and communication outreach
- Implement natural history study to better understand pathogen(s), pathogenesis and long-term outcomes
- Continue close dialogue with parents and families on a variety of issues
  - Medical record interoperability

Questions for BSC

- Do you agree with themes?
- Any other areas to consider?
- Suggestions for ways to increase engagement of clinicians and public health?

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