Multisystem Inflammatory Syndrome in Children (MIS-C)

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Acknowledgments

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Multisystem Inflammatory Syndrome in Children (MIS-C)

Children are falling ill with perplexing inflammatory syndrome thought to be linked to covid-19

Number of cases remains small, but officials are on high alert because of severity

For Parents: Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19

Young adults are also affected by Kawasaki-like disease linked to coronavirus, doctors say
MIS-C Clinical Presentation

• Fever (>38.0°C for ≥24 hours)
• Laboratory evidence of inflammation
• Clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
• Positive for current or recent SARS-CoV-2 infection or COVID-19 exposure within prior 4 weeks
• Observed variations
  • Full blown MIS-C (critically ill, in ICU)
  • Milder version of MIS-C (hospitalized, but not in ICU)
  • Significant respiratory involvement
  • Classic Kawasaki disease
Research Platform to Understand MIS-C

AT-RISK PEDIATRIC COVID-19 COHORT
Goal: Large cohort to advance understanding of pediatric SARS-CoV-2 spectrum of illness

LONG-TERM FOLLOW UP
Goal: Ascertain outcomes, treatment effects, and long term, multisystem complications of MIS-C

MIS-C COHORT PLATFORM
Goal: Comprehensive understanding of phenotypes, natural history, outcomes, pathobiology of MIS-C

Streamlined common data protocol, collection, robust cloud-based data sharing
MIS-C COHORT PLATFORM

Goal: Comprehensive understanding of phenotypes, natural history, outcomes, pathobiology

- Longitudinal follow-up (e.g., echo core lab)
- Adaptive design trials and trial prep (PK/PD studies)
- Deep phenotyping: WGS, RNA seq, Antibody profiling, etc.
- Data platform to support access and computation
- Data Coordinating Center to aggregate data
- Leveraging and linking existing cohorts and networks
Pediatric Trials Network

• **Purpose**: Gather information on pharmacokinetics and safety of several drugs not typically used in children to define appropriate dosing of these drugs for COVID-19

• Incorporated opportunistic study of six drugs into an existing protocol:
  - Azithromycin, Chloroquine, Hydroxychloroquine, Lopinavir/Ritonavir, Ribavirin, and Tocilizumab
  - Can add more as they are implemented into care of children

• Partnered with nearly 50 study sites across the country to collect blood samples to
  - Characterize pharmacokinetics of these drugs across the pediatric age range
  - Collect information on drug safety and clinical course (e.g., date(s) of positive testing; duration and type of respiratory support; duration of hospitalization; mortality)
  - Develop partnerships with PIs around the country who are exploring the safety and efficacy of hydroxychloroquine and/or azithromycin
AT-RISK PEDIATRIC COVID-19 COHORT
Goal: Large cohort to advance understanding of pediatric SARS-CoV-2 spectrum of illness

- Up to 10,000 SARS-CoV-2 positive children and adolescents
- Build on existing clinical trial network infrastructures
- Basic genetic and immunophenotyping studies
- Use EHRs, minimal testing and case report forms
- Control group for MIS-C and those who develop severe but typical COVID-19
- Smaller group with COVID-19: deep phenotyping and more extensive clinical data to understand disease manifestations and progression
- Leverage RADx PREVAIL study: develop novel or non-traditional approaches (e.g., diagnostic and prognostic biomarkers) to identify and characterize the spectrum of MIS-C and predict the longitudinal risk of disease severity after SARS-CoV-2 exposure
LONG-TERM FOLLOW UP STUDY
Goal: Ascertain outcomes, treatment effects, and long term, multisystem complications of MIS-C

- Multi-system testing (e.g., cardiac, neurological, GI, respiratory)
- Immunological testing
- Immune response and vaccine considerations
COVID-19 and Pregnancy

- NICHD’s Maternal Fetal Medicines Unit (MFMU) launched a study
  - Currently can support enrollment of 21,000 pregnant women over 12 sites
  - Goal is to compare overall antenatal care, maternal health complications, rates of C-sections and maternal mortality in pre- and post- COVID-19 eras
  - Includes natural history study of 1,500 COVID-19+ pregnant women
  - Developed common data elements (CDEs) with other NICHD networks
  - Encouraging other registries adopt these CDEs to aid future meta-analyses
- Discussions occurring with outside organizations for potential collaborations on registry efforts for pregnant women and newborns
- Advocating for inclusion of pregnant women and children in major trans-NIH initiatives such as ACTIV and RADx that involve clinical trials of therapeutic vaccines and rapid testing
Questions?