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CRR 8/3/18

Title: Development of a Clinical Database and Biobank for Investigation of neuroinfectious diseases and neuroinflammatory conditions

AIM:
The encephalitides associated with antibodies against cell-surface or synaptic proteins are a new category of diseases that occur with focal or widespread involvement of the central nervous system. These antibodies have been shown to target extracellular epitopes of neuronal cell-surface or synaptic proteins. In many cases of suspected autoimmunie encephalitis the underlying antigen/antibody is not identified making the diagnosis more challenging. Given that these syndromes often respond to immunotherapy, resulting in substantial or complete recovery in 70–80% of the patients, it is important further investigate clinical and laboratory data to identify patterns/similarities amongst cases of patient with neuroimmunologic disease to accurately diagnosis cases of autoimmune encephalitis. Recent studies have showed that 14% of patients with anti-NMDAR encephalitis did not have detectable antibodies in serum using two different techniques, while all had antibodies in the CSF. For other disorders, the proportion of cases that are CSF positive and serum negative is unknown.

The purpose of this study is to develop a clinical database and repository of blood and spinal fluid samples from people being evaluated or treated for infectious and/or inflammatory conditions that impact the brain and/or spinal cord. Patients without a known diagnosis will also be entered into this database in order to foster future research. Infectious and/or inflammatory nervous system conditions of interest include Multiple Sclerosis (MS), Transverse Myelitis (TM), Acute Disseminated Encephalomyelitis (ADEM), Neuromyelitis Optica (NMO) or Optic Neuritis (ON), NMDAR encephalitis, neuropsychiatric syndromes associated with lupus (CNS lupus), primary central nervous system (CNS) vasculitis, Human Immunodeficiency Virus (HIV) or other infections of the nervous system that impact the brain and/or spinal cord.

The Department of Neurology at Columbia University Medical Center evaluates hundreds of patients a year with various infectious diseases and inflammatory conditions. Many of these diseases need improved diagnostic methods since fast and accurate diagnosis remains the essential building block for new treatments. The development of a comprehensive clinical database and repository of blood and spinal fluid samples of cases of neuroinflammatory conditions and/or neuroinfectious diseases will allow us to perform studies to evaluate inflammatory markers and develop new diagnostic technologies. Additionally, the development of a repository will allow us to collaborate in a multidisciplinary manner, across many centers.

The goal of my project is to identify pediatric cases of suspected autoimmune encephalitis with an unidentified antibody that present to Morgan Stanley Children's Hopsital or visits at the pediatric neurology practice at Columbia Doctors in Harkness Pavilion 5th floor or 3rd Floor Vanderbilt Subspecialties clinic affiliated with New York Presbyterian and to consent patients and coordinate with primary teams to collect an additional tube of CSF/blood for further analysis of CSF and serum antibody profiles to identify new biomarkers patterns.

STUDY DESIGN:
Participation Duration:
5 years
Anticipated Number of Subjects:
500

In this study we will be indentifying patients diagnosed with neuroencephalitis. Information to be collected will include clinical information from charts including initial presentation, workup (both inpatient and outpatient), initial and maintenance treatment regimens, level of acuity, duration of

hospitalization, and clinical outcome at last follow up. We will also collect information on rehabilitation outcomes. CSF and blood will be collected during the course of their clinical care and placed into our repository for future research studies. Medical records will be reviewed on a regular basis to ensure up to date data. The repository samples will be stored and used for Genetic Testing such as single cell RNAseq in the future. The sample will be stored for as long as deemed useful for research purposes. For our adult samples the desired amount of CSF fluid is 5-10 mL and residual volume will be used if available, if not, an additional amount of cerebrospinal fluid/serum will be drawn to get desired amount. If additional lumbar punctures or blood draws are performed, 5-10 mL of CSF/serum will be collected as well. For identification purposes, patients will be assigned a unique identifying code, which will be placed on all the material that is sent to the research laboratories for confidentiality purposes. Frequencies of characteristics within different patient groups will be compared using the Chi-squared test or fisher exact test for assessment of categorical variables in the study.

Risks
There is a small risk that people not working on the study could see personal health information.
Risks and Benefits of Future Contact: There may be both risks and benefits to consenting to future contact.
The potential risks include: Participants in the study may become upset to learn that they have a greater chance of having a disease or condition. Even if genetic tests show that participants do not have a greater risk of disease, participants may still be upset if they know that others in their family have that higher risk.

Benefits
There will be no direct medical benefit to the subject; however it is possible that someone may benefit in the future.

Risks and Benefits of Future Contact: There may be both risks and benefits to consenting to future contact.

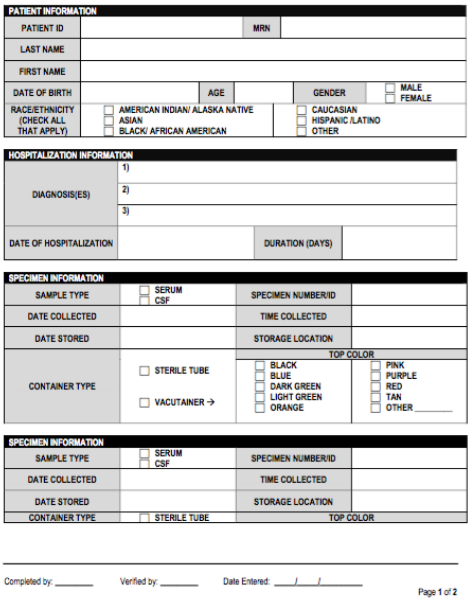
The potential benefits include: Subjects may benefit from the knowledge that they or their family have a predisposition to a certain disease or condition. This knowledge may help subjects make informed decisions concerning lifestyle and health care. This sample could one day lead to discoveries using methods and tests not yet developed.

Alternatives
Subjects may choose not to take part in this research study. Subjects do not have to take part in this study to get treatment for their condition.

Compensation
Subjects will not receive any payment or other compensation for taking part in this study.

Voluntary Participation
Participation in this study is voluntary. Refusal to participate will involve no penalty or loss of benefits to which subjects are otherwise entitled. Subjects may discontinue participation at any time without penalty or loss of benefits to which subjects are otherwise entitled.

Appendix A: Data Collection Form



PATIENT INFORMATION					
PATIENT ID		MRN			
LAST NAME					
FIRST NAME					
DATE OF BIRTH		AGE		GENDER	☐ MALE ☐ FEMALE
RACE/ETHNICITY (CHECK ALL THAT APPLY)	☐ AMERICAN INDIAN/ ALASKA NATIVE ☐ ASIAN ☐ BLACK/ AFRICAN AMERICAN		☐ CAUCASIAN ☐ HISPANIC /LATINO ☐ OTHER		

HOSPITALIZATION INFORMATION			
DIAGNOSIS(ES)	1)		
	2)		
	3)		
DATE OF HOSPITALIZATION		DURATION (DAYS)	

SPECIMEN INFORMATION			
SAMPLE TYPE	☐ SERUM ☐ CSF	SPECIMEN NUMBER/ID	
DATE COLLECTED		TIME COLLECTED	
DATE STORED		STORAGE LOCATION	
CONTAINER TYPE	☐ STERILE TUBE ☐ VACUTAINER →	TOP COLOR: ☐ BLACK ☐ BLUE ☐ DARK GREEN ☐ LIGHT GREEN ☐ ORANGE ☐ PINK ☐ PURPLE ☐ RED ☐ TAN ☐ OTHER _____	

SPECIMEN INFORMATION			
SAMPLE TYPE	☐ SERUM ☐ CSF	SPECIMEN NUMBER/ID	
DATE COLLECTED		TIME COLLECTED	
DATE STORED		STORAGE LOCATION	
CONTAINER TYPE	☐ STERILE TUBE	TOP COLOR	

Completed by: _____ Verified by: _____ Date Entered: ____/____/_____

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References:
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2. Thakur K, Motta M, Asemota A, et al. Predictors of Outcome in Acute Encephalitis. Neurology 2013;81(9):793-800
3. Thompson H, Thakur K. Infections of the Central Nervous System in Returning Travelers and Immigrants. Curr Infect Dis Rep. 2017 Oct 3;19(11):45. doi: 10.1007/s11908-017-0594-5.
4. Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for longterm outcome in patients with antiNMDA receptor encephalitis: an observational cohort study. Lancet Neurol 2013;12:157165.
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