Collection of various sample types from patients with rare/emerging or exotic viruses and Rickettsia for molecular and serological diagnostic test development and validation purposes.

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1, to create a sample pool for future diagnostic test development and validation; 2, to compare various sample types in molecular and serodiagnostic tests of rare/emerging or exotic viruses and Rickettsial infections in order to test their...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON54440

Source
ToetsingOnline

Brief title
iMONSTER

Condition

- Other condition
- Viral infectious disorders

Synonym
exotic and/or emerging arboviral and other infection, rare and exotic diseases from which some are transmitted by mosquito and other insects

Health condition

Rickettsial infection

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: biobank, diagnostic test development, rare/emerging and exotic diseases and Rickettsia

Outcome measures

Primary outcome

Primary end point: creation of a sample pool for diagnostic test development

and validation of rare/emerging or exotic viruses and Rickettsia.

Secondary outcome

Secondary end points:

1, to gain knowledge about the kinetics of viral infections and Rickettsiae spp

infection;

2. to test the suitability of body fluids and eschar swab for diagnostic use;

3. concordance between PCR test results, virus isolation and (neutralizing)

antibody (IgM, IgG) responses;

4. presence and persistence of other markers (e.g. IgM, IgG, IgA, IgE).

Study description

Background summary

Infectious diseases present one of the most significant health and security

challenges to the global community. Due to increased mobility, climate change and advanced technology we see and detect increasing amount of rare/(re)emerging and exotic diseases. All important questions arising with an emerging infection (like source and route of transmission, infectivity of patients, recommendation of safety measures for health care personal and distribution in an animal reservoir or vectors) require high quality and validated laboratory diagnostic assays. To be able to detect and distinguish pathogens we need to have knowledge about their RNA or DNA sequence, genetic diversity and antibody kinetics as well as suitable and well verified/validated diagnostic tests. Before implementation into daily diagnostics a test has to be verified/validated on a representative sample set and using verified positive controls. However these samples are scarce and an international standard material which could aid standardisation and harmonisation of results rarely exist [1].
To investigate the patient*s infection, commonly a blood sample is taken for pathogen detection. The test used can be a PCR or for a test demonstrating the presence of specific antibodies/antigens. The use of saliva and urine for the diagnosis for many viral infections has been reported, however, it is often not performed in the broad routine diagnostics. Sampling of blood requires medically trained personal and can cause discomfort to the patient. Therefore, the sampling by non-invasive methods (e.g. saliva, urine, faeces) might be a very valuable alternative for investigating a disease. This is supported by the report on continuing viremia in urine or semen of yellow fever infected patients, extending the period for the use of more specific molecular detection techniques and sequencing. Additionally, carriage in semen provides important information as it can lead to sexual transmission, like was found for Ebola and Zika virus [2]. Zika virus was also isolated from rectal swabs [3] pointing out another route of dissemination and potential sexual transmission. Diagnoses of several tick-borne emerging pathogens such as tick-borne encephalitis virus and Rickettsiae spp currently rely on changes in specific antibody detection in convalescent blood samples, consequently delaying diagnosis for weeks. In addition, interpretation of these serology results is complicated by extensive cross-reactivity of antibodies and aspecific reactions. To optimise serological tools for Rickettsia, PCR confirmation on early specimen (eschar swab and whole blood) is essential as a gold standard. . Furthermore the length of persistence for (neutralizing) antibodies especially for newly emerged pathogens is not known.

A recent review summarizes the current knowledge about the various sample types used for some of the recently emerged viruses like Dengue, Chikungunya, Ebola, other Flaviviruses like Zika, West Nile and Yellow Fever and other viruses causing haemorrhagic fever [2] and clearly highlights the knowledge gaps regarding presence and persistence of these pathogens in various body fluids.
The gaps and importance of the above knowledge gaps described was also recognised at the European level and the PREPARE project, which is an EU funded network for harmonized large-scale clinical research studies on infectious diseases, was initiated (one of the work packages is focusing on arboviruses).

Therefore, we propose a study in which patients with strong clinical suspicion or confirmed infection with a rare/emerging/exotic virus including Rickettsiae spp infection will be approached to donate various sample types (Appendix 1). These samples will be used for two purposes: 1, to create a panel of samples which can be used for diagnostic test development and validation; 2, to gain knowledge about carriage and to test suitability for diagnostic use e.g. the presence (and duration), quantity of these pathogens and antibodies in various bodily fluids. Furthermore, parallel to this application, a non-WMO proposal was being prepared (entitled: Blood donation by volunteers to validate diagnostic tests for infectious diseases; MEC-2021-0039) which serves as a complementary to this effort. All these add a prospective approach to the already approved non-WMO protocol (2015-306) which allows the use of patient residual material for research and improvement of diagnostics.
As a tertiary care center with well-known expertise in tropical medicine, Erasmus MC is well equipped to test and diagnose patients with rare or emerging pathogens as they are often referred. The Viroscience department is one of the national reference laboratories and WHO collaborating center for *Emerging and Dangerous Pathogens of international importance, including outbreaks of Arboviruses, Viral Haemorrhagic Fevers and novel and emerging infectious diseases* hence we are experienced in diagnosing these pathogens. An important part of our responsibilities is commitment to preparedness. Material and knowledge gained from this study would be shared with our international network but only following the appropriate Material Transfer Agreement (MTA) leading to improved diagnostic worldwide. All these taken together represent a unique opportunity to conduct this study.

REFERENCES
1. NIBSC.
2. Niedrig M, Patel P, El Wahed AA, Schadler R, Yactayo S. Find the right sample: A study on the versatility of saliva and urine samples for the diagnosis of emerging viruses. BMC Infect Dis 2018; 18:707.
3. Botto-Menezes CHA, Neto AM, Calvet GA, et al. Zika Virus in Rectal Swab Samples. Emerg Infect Dis 2019; 25:951-4.

Study objective

1, to create a sample pool for future diagnostic test development and validation;
2, to compare various sample types in molecular and serodiagnostic tests of rare/emerging or exotic viruses and Rickettsial infections in order to test their suitability for diagnostic use and study length of persistence.

Study design

Single center observational study

Study burden and risks

This study entails minimal harm. Most sampling is non-invasive, although still the sampling procedures would probably represent some level of patient burden. Enrolled patients will be asked to provide a standard specimen set consisting of blood (separated in whole blood, dry blood spots, serum), urine, faeces, saliva) and as optional specimen the following: sweat, tears, breast milk, vaginal swab/semen, post-partum placenta biopsy, eschar swab. Follow-up samples will be asked either until patient is discharged from hospital or at follow-up control appointments if they will be scheduled due to original illness. Only adults will be approached, minimal patient information, travel and vaccination records, symptom onset and other relevant comorbidities like suppressed status will be asked in a questionnaire. In order to be enrolled in the study, the patient will need to give informed consent and will have an all-time opt-out option.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

*adult and fully capable person
*written informed consent provided
*strong clinical suspicion by infectious disease clinical specialists of infection with rare/emerging or exotic viruses or Rickettsiae spp based on signs and symptoms in combination with relevant travel history and/or activities presenting at any departments or out-patient clinic of the EMC or confirmed positive external patients/participants (Figure 1, Appendix 1 and 2). Patients will be approached and included by infectious disease clinical specialists, by their treating physician or through municipal public health services or recruited via advertisement.

Exclusion criteria

*written Informed consent NOT provided
* <18 year old

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2021
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	02-03-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-08-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL74790.078.20