Risk factors, clinical course, presence and persistence of virus in various bodily fluids, and risk of sexual transmission among U.S. adults with Oropouche virus disease

Request for OMB approval of a New Information Collection

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Supporting Statement B

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1. Respondent Universe and Sampling Methods

This is a descriptive investigation conducted in the setting of an emerging public health threat. It is impossible to predict or ensure enrollment of a specific number of participants. Given the dearth of existing information on symptoms, risk factors, viral shedding, and possibility of sexual transmission for Oropouche virus (OROV), enrollment of even a few participants will substantially increase knowledge of the topic and lead to improved public health recommendations. If possible, enrollment of larger number of participants is desirable as it will allow more precise estimates of the frequency, consistency, and duration of viral shedding. For practical purposes, investigation enrollment will be capped at 250 participants. Assuming full enrollment and participation, this sample size would detect a viral shedding or symptom prevalence of 5% with a 95% confidence interval of +/- 3% at any specific time point in the investigation.

The purpose of this information collection is not to make statistical generalizations beyond the particular respondents.

Inclusion Criteria

1. Adults 18 years of age or older who are US residents AND
2. Diagnosed with OROV disease according to the interim case definitions for confirmed and probable cases including diagnosis with a CLIA-approved testing method and with symptom onset ≤3 months prior to enrollment OR
3. Have not traveled to an area with recent OROV human disease cases (as indicated on this risk map) since January 1, 2023 and who have had sexual contact with a travel-associated case-patient (see criteria 2) in the six weeks after the case-patient's symptom onset.

Enrollment/Participant Identification

CDC will work with state health departments to determine if any individuals who either are reported as OROV disease cases to ArboNET, the national surveillance system for arboviral diseases, or have samples submitted to CDC that test positive for OROV infection meet the inclusion criteria.

For all individuals diagnosed with OROV disease who meet the inclusion criteria, investigation staff from either a state, territorial, local, or tribal (STLT) health department or CDC will contact cases. If CDC staff will be contacting cases, ask STLT health departments to distribute information (email

informational flyer or read aloud: Attachment 8) explaining the investigation and notifying patients to expect contact from CDC.

Upon initial contact, patients who meet inclusion criteria will be informed of the purpose and procedures for the investigation. If a patient is incapacitated and unable to be interviewed, their healthcare proxy/surrogate can be interviewed. If a patient declines to provide additional data, they will be thanked for their time and this should be noted on the case tracking form.

Investigation staff will read the consent statements (Attachments 9–11) and obtain verbal consent from participants over the phone. Consent will be requested separately for each component of the project (clinical information, specimen collection, and contact tracing); participants can participate in any components that they choose, or none if they do not want to. Participants will be given time to ask any additional questions they have. Frequent Q&A will be provided to investigation staff to assist with answering participants' questions (Attachment 8).

2. Procedures for the Collection of Information

All individuals who will be interacting with patients will undergo training to understand the investigation protocols, consent process, data collection tools, and how to collect these data. Each team member will have access to a secure folder for the investigation team. In this folder, they will find a tracking sheet with all confirmed and probable Oropouche virus disease cases. The tracking spreadsheet will be used to keep monitor who has been contacted, consented for investigation components, and interviews and specimens collected.

At least 3 attempts should be made to contact the patient. This should include attempts on at least 2 separate days and at different times of the day. Any time an investigation team member is unable to contact a patient they will leave a voicemail (if voicemail is set up). If after 3 attempts a patient cannot be reached; this will be noted on the tracking form.

Enrollment:
Patients will be enrolled to participate in investigation activities based on the duration since initial symptom onset and which activities they consent to. We will attempt to enroll eligible patients with confirmed or probable Oropouche virus disease and symptom onset ≤3 months prior.

The following activities will be completed as soon as possible after enrollment:

1. Interview participant using the initial clinical and risk factors survey (Attachment 3) and, if applicable, provide them with a symptom diary (Attachment 5) to record details on symptoms daily.
2. Initial specimen collection (see "Specimen Collection" section below)
3. Interview participants to identify sexual partners between their return from international travel and time of interview (maximum of 6 weeks post symptom onset) using Attachment 6 and obtain permission to reach out to those sexual contacts.
4. Interview sexual contacts of patients using Attachment 7 to determine if they had a clinically compatible illness after sexual contact with an OROV disease patient.

a. Obtain consent to collect a serum sample from sexual contacts who reported being symptomatic to test for the presence of RNA or neutralizing antibodies to OROV, depending on time from symptom onset to sample collection.
    i. If, after testing, contact meets case definition for confirmed or probable OROV disease, attempt to enroll in symptom and specimen collection components of investigation.

Follow-up:
The following activities will be completed weekly for the first four weeks after symptom onset, and then every two weeks until 12 weeks after symptom onset:

1. Complete abbreviated clinical survey (Attachment 4) until participant reports no symptoms for 4 weeks
2. Complete specimen collection (see "Specimen Collection" section below)

Time points for data and specimen collection will allow for 4 days on either side of the collection date. For example, if 8 weeks post onset is September 20, week 8 samples and/or symptoms could be collected from September 16 through September 24.

If participants miss a time point, we will still attempt to collect specimens and symptoms at the next scheduled time point, but they will not be included in calculating frequencies of symptoms or viral RNA positivity for the missed time point.

Specimen Collection

Participants in the sample collection investigation will be asked to donate blood, semen or vaginal secretions, urine, and saliva. All sample types will be collected weekly through 4 weeks post symptom onset. Then, all specimen types except for blood will be collected every two weeks until 12 weeks after symptom onset. If a case patient reports breastfeeding during initial interview, they will be asked if they consent to submit a sample of breast milk for OROV testing, but breast milk will not be collected repeatedly. Participants can refuse to submit any of the specimen types.

Blood (whole blood and serum) will be collected at local or state health department clinics. If the patient does not live near a health department clinic or the health department does not have capacity to collect blood, alternative blood collection sites include the patient's physician's office or using a contracted phlebotomy service. Other specimens are to be collected by the participant at home, with plain language instructions on sample collection, all equipment needed to collect samples, and box with prepaid shipping labels and ice packs provided to the participants via mail. Urine will be collected prior to semen or vaginal secretion samples.

Specimens will be shipped to CDC's Arboviral Diseases Branch in Fort Collins, CO. Surveillance testing using real-time reverse transcription-polymerase chain reaction (rRT-PCR) will be performed on whole blood, semen, vaginal secretions, urine, saliva, and breast milk specimens to detect OROV viral RNA. Viral culture will be attempted on specimens that are positive on rRT-PCR and have a cycle threshold (CT) value that indicates the potential for intact virus (e.g., CT value <32). Serum specimens will undergo diagnostic testing by either rRT-PCR or plaque reduction neutralization testing (PRNT), depending on the timing of specimen collection in relation to symptom onset.

Data Collection Tools

Initial Clinical Survey (Attachment 3): this tool collects information including demographics, signs and symptoms experienced up until that time (e.g., onset, what symptoms were experienced, severity of disease, recurrence of symptoms), underlying conditions/medical history, travel history, and potential risk factors for infection during travel (e.g., outdoor activities, time spent outdoors, insect repellent use).

Follow-up Clinical Survey (Attachment 4): this tool will collect information on symptoms experienced since the participant's most recent clinical survey, including onset, recurrence and duration, and specific signs and symptoms. This tool will help determine if specific symptoms are ongoing or have recurred since previous surveys.

Symptom Diary (Attachment 5): in order to reduce recall bias in follow-up clinical surveys, this tool will be distributed to participants so they can record details on specific symptoms they experience on a daily basis. This tool will be used to complete the Follow-up Clinical Survey.

Contact Tracing Survey (Attachment 6): this tool will collect the number of sexual partners (who did not travel) between returning from travel and 6 weeks post symptom onset and then for each sexual partner will collect information on the timing and type of sexual contact, use of condoms or other barrier contraception, and contact information for eligible sexual partners.

Sexual Contact Interview (Attachment 7): this tool will be used to interview sexual contacts to confirm that they had no recent travel history to places with local transmission of OROV, and to see if they had any symptoms consistent with OROV disease within 2 weeks after any sexual contact with the case patient. This information will identify possible instances of sexual transmission of OROV so we can ask sexual contacts to submit a blood specimen for OROV testing.

3. Methods to maximize Response Rates and Deal with No Response

If participants agree, investigation staff will send reminders via text message about upcoming specimen collections and follow-up calls. If participants do not answer calls during scheduled follow-up time windows or are not prompt (i.e., within 7 days after receipt of package) with returning data/specimens they will be contacted by investigation staff via phone up to 3 times to remind them. Investigation staff may leave voicemails as a reminder on any phone call attempts.

4. Tests of Procedures or Methods to be undertaken

No pilot testing or pre-testing will be done.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

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