Rare Disease of Public Health
Significance

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance
1. To understand the epidemiology of emerging and uncommon diseases in Washington State residents and to inform public health and healthcare organizations about conditions that have been diagnosed in residents.
2. To assist in the diagnosis and treatment of cases.
3. If applicable, to identify potentially exposed close contacts, healthcare workers, and laboratory personnel and to provide counseling.
4. To identify sources of transmission and to prevent further transmission.
5. To raise the index of suspicion of a possible bioterrorism event if no natural exposure source is identified.

B. Legal Reporting Requirements
The requirements below relate to rare conditions without separate guidelines.
1. Healthcare providers: *Burkholderia mallei* and *B. pseudomallei*, emerging conditions with outbreak potential, monkeypox, MERS-CoV, SARS, smallpox, vancomycin-resistant *Staphylococcus aureus* (VRSA), or viral hemorrhagic fever agents **immediately notifiable to local health jurisdiction**; prion disease or varicella-associated death notifiable in 3 days; other rare diseases notifiable in 24 hours.
2. Healthcare facilities: *Burkholderia mallei* and *B. pseudomallei*, emerging condition with outbreak potential, monkeypox, MERS-CoV, SARS, smallpox virus, vancomycin-resistant *Staphylococcus aureus*, or viral hemorrhagic fever agents **immediately notifiable to local health jurisdiction**; prion disease or varicella-associated death notifiable in 3 days; other rare diseases notifiable in 24 hours.
3. Laboratories: *Burkholderia mallei* and *B. pseudomallei*, MERS-CoV, SARS-associated coronavirus, smallpox, vancomycin-resistant *Staphylococcus aureus* or viral hemorrhagic fever **immediately notifiable to the local health jurisdiction**; other rare disease agents notifiable in 24 hours.
4. Veterinarians: **Suspected human cases of Burkholderia mallei or B. pseudomallei immediately notifiable to the local health jurisdiction**; animal cases of some conditions notifiable to Washington State Department of Agriculture (see: http://app.leg.wa.gov/WAC/default.aspx?cite=16-70).
5. Local health jurisdictions: *Burkholderia mallei* and *B. pseudomallei*, emerging condition with outbreak potential, MERS-CoV, SARS, smallpox, VRSA or viral hemorrhagic fever **immediately notifiable to the Washington State Department of Health (DOH) Communicable Disease Epidemiology (CDE) at 206-418-5500 or 877-539-4344.**
C. Local Health Jurisdiction Investigation Responsibilities

1. Responsibilities are dependent on the disease under investigation. Report any immediately notifiable condition to Communicable Disease Epidemiology.

2. Report any case to CDE through the Public Health Issues Management System (PHIMS) as a Rare Disease of Public Health Significance, including species or organism.

2. THE DISEASES AND THEIR EPIDEMIOLOGY

Rare diseases with separate guidelines and separate PHIMS data entry screens or forms include: anthrax, arboviral diseases (e.g., dengue, western equine encephalitis), brucellosis, carbapenem-resistant Enterobacteriaceae documented to be carbapenemase-positive, cholera, coccidioidomycosis, cryptococcosis (\textit{C. gattii} only), hantavirus infection, influenza-associated death, MERS-CoV, human infection with novel influenza, plague, polio, prion disease, Q fever, human rabies, and vancomycin-resistant \textit{S. aureus} and other highly resistant organisms, viral hemorrhagic fever, West Nile virus, yellow fever, and cases for the category Unexplained Critical Illness or Death.

This guideline covers additional conditions that are rare in Washington State; exposures may be within or outside of Washington. According to the 2011 revision of Washington Administrative Code (WAC) 246-101, the conditions may be explicitly included in the WAC case definition for rare disease of public health significance; may be specified as notifiable in the WAC’s individual tables for healthcare providers, healthcare facilities, laboratories or veterinarians; or may be communicable diseases that would be of general public concern if detected in Washington. With the exceptions noted above, the conditions are generally sufficiently rare that a separate guideline has not been developed. Conditions that should be reported to Communicable Disease Epidemiology (CDE) as Rare Diseases of Public Health Significance include:

- African sleeping sickness\(^{A}\)
- Amebic meningitis
- Babesiosis*
- \textit{Burkholderia mallei} and \textit{B. pseudomallei} (glanders or melioidosis)
- Chagas disease\(^{A}\)
- Ehrlichiosis and Anaplasmosis\(^{A}\)
- Emerging condition with outbreak potential
- Histoplasmosis\(^{A}\)
- Monkeypox
- Paragonimiasis\(^{A}\)
- Severe acute respiratory syndrome-associated coronavirus disease (SARS)
- Smallpox
- Tick paralysis *
- Typhus
- Vaccinia transmission*
- Varicella-associated death*
- Viral hemorrhagic fever agents

* Condition endemic to the state recently identified in a WA resident
\(^{A}\) Condition not known to be endemic to the state recently identified in a WA resident
Additional rare conditions being investigated can be included in this category for the convenience of local health jurisdictions to document their work load and may be reported to Communicable Disease Epidemiology through PHIMS if desired. The Washington State Annual Communicable Disease Report has a summary of cases:

3. CASE DEFINITIONS

There are national cases definitions for some rare conditions including: SARS, smallpox, histoplasmosis, and varicella-associated death. Definitions can be found at:

4. DIAGNOSIS AND LABORATORY SERVICES

Appropriate diagnostic testing depends on the suspected agent. Commercial laboratory tests may be unreliable for many of these rare diseases so confirmation by a reference laboratory may be appropriate. See Section 6 for brief reviews of diagnostic testing for selected conditions. Consult with Communicable Disease Epidemiology (CDE) for assistance with diagnosis and testing (206-418-5500).

Note that Washington State Public Health Laboratories (PHL) require all clinical specimens have two patient identifiers, a name and a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

Consult with CDE regarding appropriate shipping temperature. Use the applicable PHL form. Also see:
http://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/PublicHealthLaboratories/MicrobiologyLabTestMenu

Microbiology and Parasitology form:

Serology/Virology form:
http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf

5. ROUTINE CASE INVESTIGATION

The case investigation depends on the suspected agent, its mode of transmission, and its communicability. In general, evaluate the diagnosis for a reported case including obtaining copies of laboratory reports. Call Communicable Disease Epidemiology (CDE) to arrange confirmatory testing (206-418-5500). Determine if others are at risk, either by sharing the case’s exposure or by being exposed to a case. See Section 6 for brief descriptions of investigations for selected conditions. Consult with CDE for assistance with performing a public health investigation for other agents. The reporting form for Rare Disease of Public Health Significance is available at:
http://www.doh.wa.gov/Portals/1/Documents/5100/210-067-ReportForm-Rare.pdf

Infection control measures depend on the suspected agent (see Section 6). Healthcare settings should institute airborne precautions for suspected SARS, smallpox, vaccinia, and varicella. Consult with CDE if needed.
6. MANAGING SPECIFIC DISEASES

Below are brief descriptions of select rare conditions endemic to this country or of public health concern that should be reported in Washington. Conditions with a national case definition list year of last revision: [http://wwwn.cdc.gov/nndss/](http://wwwn.cdc.gov/nndss/). Testing availability at Department of Health (DOH) or CDC is indicated. Carbapenem-resistant Enterobacteriaceae documented to be carbapenemase-positive, *C. gattii*, coccidioidomycosis, prion disease and viral hemorrhagic fever have separate guidelines (see Section 2) but are reported as Rare Diseases through Public Health Issues Management System (PHIMS).

A. Primary Amebic Meningoencephalitis (*Naegleria*)

1. Disease and its epidemiology:
   - **Agent:** *Naegleria fowleri*, a free-living amoeba
   - **Illness:** acute onset of severe headache, fever, nausea, vomiting followed by stiff neck, confusion, seizures, hallucinations. Usually fatal within 3-7 days.
   - **Incubation period:** 1-14 days
   - **Differential diagnosis:** other amoebic causes, cryptococcosis, cysticercosis, bacterial meningitis, viral meningitis, intracranial hemorrhage, connective tissue disease, malignancy rabs, taeniasis, toxoplasmosis, tuberculosis
   - **Reservoir:** warm fresh water; rarely contaminated tap water or poorly maintained swimming pool or soil. In the United States mainly but not entirely southern tier states, with recent expansion in the Midwest described.
   - **Transmission:** contaminated water entering the nose by swimming, diving, facial submersion, sinus irrigation (e.g., neti pot) with passage via olfactory nerve to the brain and meninges
   - **Communicability:** none
   - **Treatment with antiparasitic agents; poor success. Provider can consult CDC 24/7 (404-718-4745 or 770-488-7100) about diagnosis and treatment including miltefosine**

2. Case definition (2016):

   **Confirmed:** Presentation of meningoencephalitis or encephalitis with laboratory confirmation (detection of *N. fowleri* antigen or nucleic acid from a clinical specimen [e.g. immunohistochemistry or PCR])

   **Probable:** Presentation of meningoencephalitis or encephalitis with supportive laboratory evidence (visualization of motile amebae in a wet mount of CSF or isolation of *N. fowleri* in culture from a clinical specimen).

3. Diagnosis and laboratory services: CDE can arrange testing at CDC

4. Routine case investigation: identify recent fresh water activities, use of undertreated pools or use of nasal irrigation systems

5. Controlling further spread: address water source
6. Routine prevention: consider nasal clips during swimming; use sterile water in nasal irrigation systems

   [http://www.cdc.gov/parasites/health_professionals.html](http://www.cdc.gov/parasites/health_professionals.html)

B. Babesiosis

2. Disease and its epidemiology:
   - Agent is hemoprotozoan (inside red cells) parasite of genus *Babesia*, most commonly *B. microti* but also including *B. duncani* (formerly WA1), which was first described from Washington State, and *B. divergens*-like agents identified in the United States.
   - Illness can be asymptomatic; symptoms include fever, chills, myalgia, arthralgia, enlarged spleen or liver, and hemolytic anemia, with more severe illness in the elderly and immunocompromised. Four locally acquired cases ever identified in Washington; 3 were *B. duncani* and one was *B. divergens*-like. One *B. duncani* case was transfusion associated, while the other 3 babesiosis cases had presumed tick exposure.
   - Incubation period variable, probably 1-8 weeks
   - Differential diagnosis: ehrlichiosis, Lyme disease, malaria relapse, spotted fevers, typhoid fever
   - Reservoir animals include rodents and small mammals
   - Transmission is usually through bites of infected *Ixodes* ticks; person-to-person transmission is rare and only by transfusion (usually from an asymptomatic donor)
   - Communicable only through transfusion
   - Treatment is with appropriate antibiotics


   **Suspect:** case with confirmatory or supportive laboratory results but insufficient clinical or epidemiologic information for classification (e.g., only a lab report)

   **Probable:**

   (a) case with supportive laboratory results AND one or more of fever, anemia, or thrombocytopenia

   **OR**

   (b) blood donor or blood recipient epidemiologically linked to a confirmed or probable case AND either:

   a. confirmatory lab evidence but without clinical evidence (i.e., no fever, anemia, thrombocytopenia, chills, sweats, headache, myalgia, or arthralgia); OR

   b. supportive lab evidence without fever, anemia or thrombocytopenia, but may or may not have one or more of the following: chills, sweats, headache, myalgia, or arthralgia.
Confirmed: a case with one or more of fever, anemia, thrombocytopenia, chills, sweats, headache, myalgia, or arthralgia AND confirmatory laboratory evidence.

Laboratory Evidence:

- **Confirmatory:** detection of *Babesia* by visualizing parasites in blood smears, PCR, nucleic acid amplification, or isolation in animal inoculation
- **Supportive:** demonstration of *Babesia* by any of the following serologic tests:
  - *B. microti* by IFA total Ig or IgG at ≥1:256 (or ≥1:64 for epi-linked blood donors or recipients)
  - *B. microti* by Immunoblot IgG positive
  - *B. divergens* IFA total Ig or IgG titer ≥1:256
  - *B. duncani* IFA total Ig or IgG titer ≥1:512

4. Diagnosis and laboratory services: DOH can confirm the agent or arrange testing at CDC. Submit blood smears, whole blood in EDTA (purple top) tube, and serum in separation or clot tube with microbiology form (Section 4).

5. Routine case investigation: Identify travel exposures, tick bites, and exposure to tick habitats with emphasis on locally acquired infection. Identify blood transfusions and test all blood donors or recipients associated with the case. The CDC case form is a guide: [http://www.cdc.gov/parasites/babesiosis/resources/babesiosis_case_report_form.pdf](http://www.cdc.gov/parasites/babesiosis/resources/babesiosis_case_report_form.pdf)

6. Controlling further spread: No isolation or restrictions apply. Case must defer donating blood for life. Educate those sharing a case’s exposure about signs and symptoms of babesiosis and encourage them to seek care if illness develops.

7. Routine prevention: When in risk areas wear long pants and a long-sleeved shirt, use tick repellent when necessary, check for and remove ticks, and monitor for symptoms.


C. *Burkholderia mallei* (glanders) and *B. pseudomallei* (melioidosis)

1. Diseases and their epidemiology:
   - Glanders:
     i. Agent is Gram-negative rod *Burkholderia mallei*; potential bioterrorism agent
     ii. Illness in humans generally includes malaise, fever, chills, fatigue, myalgia, multiple skin nodules, and regional lymphadenopathy. Inhalational exposure can result in pneumonia, pleuritic chest pain, cervical adenopathy, pulmonary abscesses or pleural effusions. Infections can cause septicemia.
     iii. Incubation period ranges 1-21 days (usual 10-14), shorter with high inoculum
     iv. Differential diagnosis: typhoid, tuberculosis, syphilis, erysipelas, lymphangitis, multiple causes of pneumonia, sepsis
v. Primarily a disease of horses, mules, and donkeys in Asia, Africa, the Middle East, and South America. Not found in environment; does not persist in water, soil, or plants. No cases in United States since the 1940s.

vi. Transmission is by contamination of open skin wounds or mucous membranes, rarely by ingesting meat or inhaling respiratory secretions. Human cases are generally from occupational exposure to animals or in a laboratory setting.

vii. Communicability occurs rarely via respiratory or cutaneous secretions

viii. Treatment is with long courses of appropriate antibiotics

- Melioidosis (Whitmore’s disease):
  i. Agent is soil/water saprophyte B. pseudomallei; potential bioterrorism agent
  ii. Illness ranges from none to bronchitis, pneumonia, cutaneous or visceral abscesses (e.g., empyema, osteomyelitis, meningoencephalitis), or septicemia
  iii. Incubation period: generally 1-21 days, shorter with high inoculum
  iv. Differential diagnosis: multiple causes of soft tissue infections, bone and joint infections, brain infections, pulmonary infections, sepsis
  v. Reservoir is soil and water, particularly in tropics and subtropics. One travel-acquired case was reported in Washington (2011); exposure was in Mexico.
  vi. Transmission is through wound infection, dust inhalation, water aspiration, contact with rodents, direct or sexual contact with a case patient, breast feeding, bloodborne, or intentional distribution; laboratory exposure can occur
  vii. Communicability of uncertain duration through blood or body fluids
  viii. Treatment is with long courses of appropriate antibiotics

2. Case definition (2012)

   **Confirmed:** B. pseudomallei isolation from a clinical specimen

   **Probable:** Meets the clinical description; has either a four-fold or greater risk in B. pseudomallei antibody titers by IHA in paired sera at least two weeks apart or evidence of B. pseudomallei DNA in specimens from a normally sterile site; and has either travel to an endemic area or known exposure to B. pseudomallei

3. Diagnosis and laboratory services: DOH does PCR and culture to confirm the agent. Submit culture with a microbiology form (Section 4).

4. Routine case investigation: notify CDE immediately for suspected or confirmed case; evaluate any laboratory exposures to those working with cultures; obtain appropriate specimens as soon as possible for testing including serum, tissues slides, or culture (consult with CDE first) with serology or microbiology form (Section 4).

5. Controlling further spread: contact precautions in medical settings. Educate those sharing a case’s exposure about signs and symptoms of glanders and melioidosis. Educate laboratory workers about appropriate precautions.

6. Routine prevention: when in risk areas for melioidosis avoid soil and water contact, particularly if open skin wounds or chronic medical condition (diabetes, renal disease)

D. Chagas disease (American trypanosomiasis)

1. Disease and its epidemiology:
   - **Agent is protozoan parasite** *Trypanosoma cruzi*
   - Illness acute phase may be asymptomatic or involve weeks to months of fever, rash, headache, body aches, eyelid swelling, loss of appetite, diarrhea, and vomiting; chronic phase usually asymptomatic but may involve enlarged heart, esophagus, or colon, causing conduction abnormalities, aneurysm, dysphagia, regurgitation, prolonged constipation, and other cardiac and gastrointestinal manifestations. Positive serology at blood donation typically reflects prior asymptomatic infection. Illness is more severe in persons with AIDS (may be cerebral chagoma) or in younger children.
   - Incubation period: 5-14 days for bug bite, 30-40 days for transfusion
   - Differential diagnosis varies with presentation: acute (leishmaniasis, malaria, meningitis), cardiac (angina/infarct, arrhythmias, dilated cardiomyopathy), intestinal (acute or chronic megacolon, esophageal abnormality, obstruction)
   - Reservoir is humans, dogs, rabbits, guinea pigs, swine, rodents, and other animals, primarily in Mexico, Central America, and South America, rarely in United States though reservoirs and vectors occur in some southern and southwestern states. In 2013 and 2015 chronic cases with exposure in South America were reported in Washington.
   - Transmission mainly by bites from triatomine bugs (reduviid or “kissing” bugs) or bug feces contaminating a wound or mucous membrane (eye), less commonly by food containing insect feces, congenital infection, blood transfusion, or organ transplant
   - Communicability only congenitally or through blood transfusion
   - Treatment for acute infection, congenital infection, reactivated infections if immunosuppressed, and pediatric chronic infections is with antiparasitic medications (nifurtimox and benznidazole available from CDC) combined with appropriate medical management of chronic complications

2. Case definition
   - **Confirmed:** Acute: parasites seen (thick or thin smears) or PCR; Chronic: clinical assessment and at least two modalities of serological tests (e.g., ELISA and IFA)

3. Diagnosis and laboratory services: If no risks, retest commercially. If risk factors, CDE can arrange testing at CDC ([https://www.cdc.gov/laboratory/specimen-submission/](https://www.cdc.gov/laboratory/specimen-submission/)). PCR assay is sometimes diagnostic and can be used to monitor after accidental or iatrogenic exposure.

4. Routine case investigation: Refer chronic case for examination and EKG. Identify travel exposures, bug bites, and exposure to bug habitats with emphasis on possible U.S.-acquired infection. Identify and test all blood donors or recipients associated with a case.
5. Controlling further spread: No isolation or restrictions apply. Case should defer donating blood if ever diagnosed with Chagas. Educate those sharing a case’s exposure about signs and symptoms of Chagas.

6. Routine prevention: in risk area use bed nets, protective clothing, and insect repellents.


https://www.cdc.gov/parasites/chagas/health_professionals/index.html

Chagas Biovigilance Network – http://www.aabb.org/research/hemovigilance/Pages/chagas.aspx

E. Ehrlichiosis and Anaplasmosis

1. Diseases and their epidemiology:
   - Agents are obligate intracellular bacteria including in North America Ehrlichia chaffeensis infection (human ehrlichiosis), E. ewingii infection (formerly human monocytic ehrlichiosis) and Anaplasma phagocytophilum infection (formerly human granulocytic ehrlichiosis or human granulocytic anaplasmosis).
   - Illness typically involves acute onset of fever accompanied by chills, headache, myalgia, malaise, anemia, leucopenia, thrombocytopenia, altered liver function, meningoencephalitis, vomiting, or rash. Travel-acquired cases in Washington residents were reported in 2004, 2007, and 2011.
   - Incubation period is 5-10 days (ehrlichiosis), 5-21 days (anaplasmosis).
   - Differential diagnosis: spotted fever rickettsiosis, bacterial or viral meningitis, relapsed malaria, typhoid fever.
   - Reservoirs for Ehrlichia are dogs and white-tailed deer; reservoirs for Anaplasma are wild rodents, ruminants, and cervids.
   - Transmission is by ticks including Ixodes species (for Anaplasma) and Amblyomma americanum (for Ehrlichia chaffeensis and E. ewingii).
   - Communicability: none.
   - Treatment is with appropriate antibiotics.


   **Suspect:** case with laboratory evidence of past or present infection with undetermined ehrlichiosis or anaplasmosis but no clinical information available.

   **Probable:** clinically compatible case with fever AND one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation; AND one of: evidence for E. chaffeensis infection by single serology positive or microscopic identification of morulae OR evidence for A. phagocytophilum infection by single serology positive OR microscopic identification of morulae OR laboratory evidence of past or present infection with undetermined ehrlichiosis or anaplasmosis.

   **Confirmed:** clinically compatible case with fever AND one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation.
transaminase elevation; AND one of: evidence for *E. chaffeensis* infection by fourfold rise in serology, culture, PCR, or immunohistochemistry OR evidence for *E. ewingii* infection by PCR OR evidence for *A. phagocytophilum* infection by fourfold rise in serology, culture, PCR, or immunohistochemistry.

3. Diagnosis and laboratory services: CDE can arrange testing. Submit blood and tissue samples with appropriate serology and/or microbiology forms (Section 4).

4. Routine case investigation: ask about travel to endemic areas, potential tick habitats, and tick bites. If endemic exposure is suspected, collect detailed location information.

5. Controlling further spread: Educate those sharing a case’s exposure about signs and symptoms of ehrlichiosis and/or anaplasmosis.

6. Routine prevention: When in risk areas wear long pants and a long-sleeved shirt, use tick repellent when necessary, check for and remove ticks, and monitor for symptoms.


### F. Histoplasmosis

1. Disease and its epidemiology:
   - Agent is *Histoplasma capsulatum*, an environmental fungus
   - May be asymptomatic, or illness may range from self-limited respiratory disease to disseminated infection. Symptoms of acute pulmonary histoplasmosis generally include fever, malaise, cough, chest pain, and myalgias.
   - Incubation is generally 3-14 days (up to 18 days documented)
   - Differential diagnosis includes other fungal pneumonias, bacterial pneumonia, *Legionella, Mycoplasma* infections, pneumococcal infections, tuberculosis, cancer, viral pneumonia
   - Transmission is generally through inhalation of spores found in soil contaminated with bird or bat droppings. Endemic areas include central and eastern United States, parts of Central and South America, Africa, Asia, and Australia. Cases have been reported in Washington in the absence of a travel history.
   - Communicability: none
   - Treatment with antifungals is indicated for moderate to severe acute pulmonary, chronic pulmonary, disseminated, and CNS histoplasmosis

2. Case definition: (2016)
   
   Clinical presentation includes at least two of the following: fever, chest pain, cough, myalgia, shortness of breath, headache, or erythema nodosum/erythema multiforme rash OR at least one of the following: abnormal chest imaging; gastrointestinal ulcerations or masses, skin or mucosal lesions; peripheral lymphadenopathy; pancytopenia; enlargement of the liver, spleen, or abdominal lymph nodes; meningitis, encephalitis, or focal brain lesion
Confirmed: A clinically compatible case with evidence of *H. capsulatum* by culture, histopathology, ≥4-fold rise in CF titers taken at least 2 weeks apart, detection of H band by immunodiffusion, documented seroconversion by detection of M band by immunodiffusion, or nucleic acid detection.

Probable: A clinically compatible case with identification of *H. capsulatum* by cytopathology, a CF titer 1:32 or greater, detection of M band without a previously negative test, or antigen detection, OR a case that meets confirmatory laboratory criteria, but no clinical information is available, OR a clinically-compatible case that does not meet laboratory criteria but is epi-linked to a confirmed case (e.g. common environmental exposure).

3. Diagnosis and laboratory services: CDE can arrange testing. Submit serum or CSF samples or fungal isolates with appropriate serology and/or microbiology forms.

4. Routine case investigation: ask about travel to endemic areas, potential exposure to soil, bird feces or bat feces. If endemic exposure is possible, ask detailed location information.

5. Controlling further spread: Educate those sharing a case’s exposure about signs and symptoms of histoplasmosis.

6. Routine prevention: Large amounts of bird or bat droppings should be cleaned up by professional companies that specialize in the removal of hazardous waste.

7. Resources: [https://www.cdc.gov/fungal/diseases/histoplasmosis/](https://www.cdc.gov/fungal/diseases/histoplasmosis/)

G. Monkeypox

1. Disease and its epidemiology:
   - Agent is monkeypox virus in the genus *Orthopoxvirus*
   - Illness is typically fever, headache, myalgia, backache, and lymphadenopathy followed by vesicular-pustular rash like smallpox; cases in Africa up to 10% fatal
   - Incubation period: about 12 days
   - Differential diagnosis: smallpox, chickenpox, shingles, measles, coxsackievirus (hand foot mouth disease), scabies, drug allergy, insect bites, rubella, syphilis, molluscum contagiosum, mononucleosis, impetigo, scarlet fever, erythema toxicum
   - Reservoir is presumed to be primates and squirrels in central and western Africa
   - Transmission is from an infected animal by bites or contact with body or rash fluids
   - Communicability: person-to-person spread can occur through respiratory droplets or body fluids
   - Treatment is supportive

2. Case definition (for 2003 outbreak)
   - **Suspect**: case with exposure (to wild animal or exotic pet) AND fever or unexplained rash AND two or more consistent signs or symptoms within 21 days of last exposure
   - **Probable**: case with exposure (wild animal or exotic pet) AND fever AND either vesicular-pustular rash within 21 days of last exposure or no rash but IgM elevated
Confirmed: case with viral isolation, PCR, electron microscopy, or immunohistochemistry confirmation

3. Laboratory and diagnostic services: CDE can arrange serology, microscopy, and confirmation of culture. Submit serum, tissues slides, or culture (consult with CDE first) with virology/serology form (Section 4).

4. Routine case investigation: notify CDE immediately for suspected or confirmed case; obtain appropriate specimens as soon as possible for testing

5. Controlling further spread: contact and droplet precautions, post-exposure smallpox vaccine for those providing direct patient care; notify Environmental Health Program for animal containment issues

6. Routine prevention: animal importation regulations

7. Resources: http://www.cdc.gov/poxvirus/monkeypox/

H. SARS (Severe Acute Respiratory Syndrome) and Novel Coronavirus Infection – See separate guideline for Middle East Respiratory Syndrome (MERS)

1. Disease and its epidemiology:
   - Agent is SARS-associated coronavirus responsible for a 2003 outbreak with 8,098 cases primarily in Asia but including 8 travel-associated cases in the United States
   - Illness is fever > 38.0°C (100.4°F) and flu-like symptoms, sometimes diarrhea, followed by cough and pneumonia; about 10% mortality for SARS
   - Incubation period: 2-10 days
   - Differential diagnosis: influenza, parainfluenza, pneumonia (bacterial, fungal, Pneumocystis, viral), MERS, psittacosis, Q fever, rhinovirus, rickettsialpox, sepsis
   - Reservoir is presumed to be wild mammals for SARS
   - Transmission is by respiratory droplets or presumably close contact with an infected animal; transmission has occurred in healthcare settings.
   - Communicability is high for certain patients with respiratory symptoms (e.g., transmission among hotel guests or to staff and patients in an emergency department)
   - Treatment is supportive

   - Probable: case with temperature >100.4°F (>38°C) AND pneumonia by x-ray or ARDS or consistent autopsy AND close contact with a confirmed case
   - Confirmed: case with fever and any consistent respiratory symptom AND antibody detection, virus isolation, or SARS-CoV RNA detection by PCR

3. Diagnosis and laboratory services: CDE can arrange testing. Use PPE for collecting multiple specimens including respiratory (nasopharyngeal wash, nasopharyngeal swab, oropharyngeal swab, bronchoalveolar lavage, tracheal aspirate, pleural fluid, sputum), stool, serum, plasma (EDTA), and lung tissue with a virology/serology form (Section 4).
4. Routine case investigation: notify CDE immediately for a suspected or confirmed case; obtain appropriate specimens as soon as possible including serum, lung tissue or respiratory secretions. Recommend appropriate personal protection when with patient; ask travel history and identify risk exposures; identify those sharing exposure with case and those exposed to case; institute isolation and quarantine measures as appropriate.

5. Controlling further spread: airborne precautions in healthcare settings, droplet precautions in home settings; consider quarantine for exposed persons

6. Routine prevention: hand and respiratory hygiene, precautions during travel to risk areas with potential exposure to live wild animals including animal markets


1. Disease and its epidemiology:
   - Agent is variola virus, considered extinct in nature; potential agent of bioterrorism
   - Illness begins as febrile flu-like illness followed by rash progressing through stages of macules, papules, vesicles, pustules, and scabs; no naturally-occurring cases worldwide since 1977
   - Incubation period: 7-19 days
   - Differential diagnosis: chickenpox/shingles, vaccinia (smallpox vaccine), measles, coxsackievirus , scabies, drug allergy, impetigo, insect bites, monkeypox, rubella, syphilis, molluscum contagiosum, mononucleosis, scarlet fever, erythema toxicum
   - Reservoir was humans, now only laboratory specimens exist
   - Transmission is through respiratory droplets and fomites or through deliberate release of weaponized material; scabs contain virus and are infectious even when dried
   - Communicability is high through respiratory secretions while lesions are present
   - Treatment is supportive; antivirals may be considered


   **Suspect**: case with fever followed in 1-4 days by generalized, acute vesicular or pustular rash
   
   **Probable**: case with acute onset of fever ≥101º F (≥38.3º C) followed by a rash characterized by firm, deep seated vesicles or pustules in the same stage of development without other apparent cause OR clinically consistent case with epi link to a confirmed case
   
   **Confirmed**: laboratory confirmed case (PCR or virus isolation) OR case with acute onset of fever ≥101º F (≥38.3º C) followed by a rash characterized by firm, deep seated vesicles or pustules in the same stage of development without other apparent cause with epi link to a laboratory-confirmed case

3. Diagnosis and laboratory services: CDE can arrange testing; submit vesicle, scab, skin, and serum specimens (consult CDE first) with virology/serology form (Section 4).
4. Routine case investigation: notify CDE immediately for suspected or confirmed case; evaluate the diagnosis particularly if lesions are deep-seated firm well-circumscribed vesicles or pustules at same stage of development. Recommend appropriate healthcare personal protective equipment. Submit with the virology/serology form (Section 4): 10 ml serum; three lesions (skin top layer, glass slide touched to scraping of lesion base, EM grid or swab touched to base of open lesion); scabs; full thickness skin punch-biopsies.

5. Controlling further spread: strict contact and airborne precautions in healthcare setting; consider quarantine for exposed persons.


J. Spotted fever rickettsiosis

1. Disease and its epidemiology:
   - Illness for RMSF begins with sudden fever, chills, severe headache, myalgia, arthralgia, and sometimes gastrointestinal symptoms followed in 80% of cases by a macular rash (starting days 2-5) spreading from wrists and ankles to the trunk. The rash may become petechial. Delirium, meningoencephalitis, or death can occur. Other *Rickettsia* species, including *R. parkeri* and *R. africae* may have similar but milder clinical presentation and may cause an eschar at the site of tick attachment. Typically 0-3 cases are reported annually in Washington; with most exposures out of state. Most cases occur April through September when ticks are active.
   - Incubation period for RMSF is 2-14 days.
   - Differential diagnosis: babesiosis, ehrlichiosis and anaplasmosis, bacterial or viral meningitis, drug allergy mononucleosis, measles, relapsing fever, streptococcal infection, syphilis, toxic shock syndrome, tularemia, typhoid, typhus
   - Reservoir: Animal hosts are dogs, opossums, wild rabbits or rodents with clinical illness in dogs and some rodents. Hard ticks are primary vectors for RMSF: Rocky Mountain wood tick (*Dermacentor andersoni*) or American dog ticks (*D. variabilis*) from woodlands, grasslands, or shrubs between wetlands and woods in the United States, including Washington. Some recent RMSF cases were associated with brown dog ticks (*Rhipicephalus sanguineus*). *R. parkeri* is associated with *Amblyomma maculatum* (Gulf Coast tick). Transmission usually requires 4-6 hours of tick attachment. There may be risk of exposure in wooded or high grass areas or to dogs.
   - Communicability: none
   - Treatment for RMSF is with tetracyclines (usually doxycycline). The case-fatality rate is 13-25% if untreated and 4% even with appropriate antibiotic treatment.

   
   **Suspect:** case with laboratory evidence of past or present infection but no clinical information available (e.g., lab report only).
Probable: fever AND one or more of rash, eschar, headache, myalgia, anemia, any hepatic transaminase elevation, or thrombocytopenia; AND presumptive laboratory evidence of elevated IgG or IgM by IFA, ELISA, dot-ELISA, or latex agglutination.

Confirmed: fever AND one or more of rash, eschar, headache, myalgia, anemia, any hepatic transaminase elevation, or thrombocytopenia; AND confirmatory laboratory evidence of fourfold increase in IgG tested by IFA, or PCR, immunohistochemistry, or culture.

3. Diagnosis and laboratory services: CDE can arrange testing at CDC. Submit serum, whole blood, and/or tissue samples with appropriate serology and/or microbiology forms (Section 4).

4. Routine case investigation: ask about travel to endemic areas, potential tick habitats, and tick bites.

5. Controlling further spread: No person-to-person transmission; educate those sharing a case’s exposure about signs and symptoms of spotted fever rickettsiosis.

6. Routine prevention: When in risk areas wear long pants and a long-sleeved shirt, use tick repellent when necessary, check for and remove ticks, and monitor for symptoms.


K. Tick paralysis

1. Disease and its epidemiology:
   - Agent is a neurotoxin secreted in the saliva of certain ticks.
   - Illness is an acute, ascending, flaccid paralysis. There may be fatigue, myalgia, numbness in the legs, and in children flu-like symptoms. Paralysis may affect breathing muscles and cause respiratory failure. About 10% of unrecognized tick paralysis cases are fatal. Cases are rare in Washington; usually 0-1 per year and most commonly during spring months in girls (with long hair) under 10 years old.
   - Incubation period is typically 4-7 days while tick feeds.
   - Differential diagnosis: botulism, polyradiculoneuritis, acute peripheral neuropathy, snakebite
   - Reservoirs in this country are *Dermacentor andersoni* (Rocky Mountain wood tick) in northwestern states and *D. variabilis* (American dog tick) in southeastern states.
   - Transmission is through an attached tick releasing saliva.
   - Communicability: none
   - Treatment: Prompt removal of the tick usually results in complete recovery within 24 hours. It is important to remove all the mouthparts, which contain the salivary glands. Oxygen therapy or mechanical ventilation may be needed.

2. Case definition:
   - Confirmed: Symptoms consistent with illness and rapid improvement of the patient upon removal of tick.
3. Diagnosis and laboratory services: none for the clinical illness; DOH will provide tick identification. Submit ticks using Microbiology form.

4. Routine case investigation: Inquire about possible exposure to ticks. Carefully check patient for ticks, especially along the hairline.

5. Controlling further spread: N/A

6. Routine prevention: When in risk areas wear long pants and a long-sleeved shirt, use tick repellent when necessary, check for and remove ticks, and monitor for symptoms. Check potentially exposed persons (especially along hair line) and promptly remove any ticks.

7. Resources: [http://www.cdc.gov/mmwr/preview/mmwrhtml/00040975.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/00040975.htm)

L. Typhus

1. Diseases and their epidemiology:
   - Agents are *Rickettsia typhi* or *R. felis* (fleaborne – endemic or murine typhus) and *R. prowazekii* (louseborne – epidemic typhus).
   - Illness is febrile rash illness for louseborne with case fatality rate up to 40% if untreated; milder illness for fleaborne. Reservoirs for fleaborne are rats (reported from tropics and subtropics), reservoirs for louseborne are humans (Andes region of South America, Burundi, Ethiopia) and rarely flying squirrels in eastern United States. Washington’s last reported case was in 1992 following travel to Asia.
   - Incubation period 7 to 14 days.
   - Differential diagnosis: ehrlichiosis/anaplasmosis, mononucleosis, leptospirosis, spotted fever rickettsiosis, syphilis, tularemia, typhoid
   - Transmission is by infected flea or louse feces entering a wound; fleas and lice typically defecate while feeding.
   - Communicability for louseborne is through the human lice.
   - Treatment is with doxycycline for both; for louseborne also use a pediculocide.

2. Case definition
   - *Probable*: Clinically compatible illness with single IgM or IgG antibody titer.
   - *Confirmed*: Clinically compatible illness with confirmatory laboratory including fourfold antibody rise, PCR positive, or positive immunohistochemical stain.

3. Diagnosis and laboratory services: CDE can arrange testing at CDC. Submit serum and tissue samples with appropriate serology or microbiology forms (Section 4).

4. Routine case investigation: notify CDE immediately for suspected or confirmed case; obtain appropriate specimens as soon as possible for testing.

5. Controlling further spread: delouse a louse-infested patient, educate those sharing a case’s exposure about signs and symptoms of typhus.


M. Vaccinia transmission

1. Disease and its epidemiology:
   - Agent is vaccinia (smallpox vaccine) virus acquired from recently vaccinated person
   - Illness involves pustules on the exposed skin or rare complications of smallpox vaccination such as ocular infection or eczema vaccinatum
   - Incubation period: undefined but probably several days
   - Differential diagnosis: chickenpox or shingles, measles, coxsackievirus (hand foot mouth disease), bacterial skin infections, scabies, medication allergy, insect bites, rubella, syphilis, mononucleosis, monkeypox, smallpox, molluscum contagiosum, impetigo, scarlet fever, erythema toxicum
   - Reservoir is vaccine, in this country currently indicated only for selected military personnel and laboratory workers. Secondary transmission occurred in Washington in 2010 and 2012 after contact with recently vaccinated military personnel.
   - Transmission is through skin contact or other close contact (sexual contact, breast feeding, sports partner, shared clothing); tertiary transmission has occurred. Dry scabs may contain infectious virus.
   - Communicability is for duration of lesions; shed scabs may contain viable virus
   - Treatment is supportive; vaccinia immune globulin, cidofovir, and investigational drugs may be needed for severe infections

2. Case definition
   - **Confirmed:** laboratory confirmed vaccinia infection in a person not receiving vaccinia immunization

3. Diagnosis and laboratory services: CDE can arrange PCR and culture to confirm vaccinia; serology confirms development of immunity. Submit serum, blood and lesion material (consult with CDE first) with virology-serology form (Section 4).

4. Routine case investigation: immediately notify CDE for a suspected or confirmed case; evaluate the diagnosis particularly if lesions are vesicles or pustules that are deep-seated firm well-circumscribed and at the same stage of development. Recommend appropriate personal protective equipment when with patient. Submit serum, blood, and lesion material with virology-serology form (Section 4). Identify close contacts likely to have received vaccinia vaccine and persons potentially exposed to the case patient.

5. Controlling further spread: strict contact precautions particularly when around unvaccinated persons, educate those sharing a case’s exposure about signs and symptoms of vaccinia infection.

6. Routine prevention: cover vaccination site, properly dispose of bandages and scabs.
7. Resources:  
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5619a4.htm  
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5925a2.htm  
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6208a2.htm

N. Varicella-associated death

1. Disease and its epidemiology:
   - Agent is varicella zoster virus (VZV)
   - Illness with chickenpox is usually mild but can result in fatal complications such as pneumonia, secondary bacterial infection, hemorrhagic complications, or encephalitis; highest risk in neonates (30% mortality for chickenpox infections) and children (0.01% mortality for chickenpox infections); rare cases in Washington
   - Incubation period: 2-3 weeks
   - Differential diagnosis: measles, coxsackievirus, bacterial skin infections, scabies, medication allergy, insect bites, rubella, syphilis, monkeypox, molluscum contagiosum, mononucleosis, impetigo, scarlet fever, erythema toxicum, smallpox
   - Reservoir is humans
   - Transmission is person to person through respiratory droplets and discharge from lesions. Dry scabs may contain viral DNA but not infectious virus.
   - Communicability is high from 2 days before rash onset until all lesions have crusted
   - Treatment is with acyclovir for severe infection

2. Case definition (2002):
   - Probable: a probable case of varicella which contributes directly or indirectly to acute medical complications which result in death
   - Confirmed: a confirmed case of varicella which contributes directly or indirectly to acute medical complications which result in death
   - (For varicella case definition see:  http://wwwn.cdc.gov/nndss/)

3. Diagnosis and laboratory services: CDE can arrange viral culture and PCR for VZV on vesicular fluid and scabs from lesions and of serum and tissue specimens from autopsy (if available). For further information regarding laboratory diagnosis see:  

4. Routine case investigation: review the clinical presentation, physical exam findings, immunization status, and exposure history. Recommend that only immune personnel obtain specimens. Submit appropriate specimens (fluid from vesicles obtained using a Dacron swab rubbed on opened lesion, scabs, serum, and tissue from autopsy specimens), with the virology/serology form (Section 4).

5. Controlling further spread: airborne precautions in healthcare settings; only personnel with documented immunity should enter the patient’s room or participate in an autopsy. Give post-exposure prophylaxis with VariZIG to high risk exposed susceptible contacts (neonates, pregnant women, immunocompromised persons) up to ten days after exposure.
6. Routine prevention: universal childhood chickenpox vaccine; adult shingles vaccine


O. Emerging condition with outbreak potential

An emerging condition is one whose incidence in humans has recently increased or threatens to increase in the near future. Of particular concern are conditions of high severity with high potential for person-to-person spread. Public health seeks to rapidly detect such conditions, control their spread, and identify risk factors for acquisition.

Newly emerging conditions have included SARS and 2009 H1N1. Until the condition is identified it cannot be specified for notifiable conditions reporting. Similarly, the transmission, laboratory testing, case definition, and control and prevention measures will have to be determined after the condition is identified. Initial healthcare provider judgment is necessary to recognize and report an unusual condition.

Report any newly identified condition with potential for person-to-person transmission.

7. ROUTINE PREVENTION

Routine prevention measures depend on the suspected agent. See Section 6 for comments about selected conditions. Consult with Communicable Disease Epidemiology for any other conditions (206-418-5500).

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UPDATES

September 2008: The definition of “rare diseases of public health significance” was made consistent with the definition provided in WAC 246-101-010.

January 2011: Section for Specific Diseases including expanded descriptions of certain rare diseases is included. Reporting requirements were revised to reflect the 2011 Notifiable Conditions Rule revision.

January 2014: Section 2 shortened, minor wording changes elsewhere.

December 2014: Viral hemorrhagic fever was removed from this guideline and a full guideline was created.

March 2015: Coccidioides was removed from this guideline and a full guideline for Coccidioidomycosis was created.

August 2015: Carbapenam Resistant Enterobacteriaceae removed from this guideline and a full guideline was created.

April 2016: Vancomycin-resistant Staphylococcus aureus moved to a separate guideline and amebic meningitis added.

February 2017: 2016 CSTE case definition added for amebic meningitis; Histoplasmosis added.