

**Differential diagnosis for a respiratory disease outbreak: Demographic and epidemiologic data**

Pathogen	Disease	Incubation period	Person to person transmission?	Means of transmission	Attack rate	Case fatality	Age groups primarily affected	Season	U.S. (temperate) regions	International regions
Adenovirus	Adenovirus	2 to 14 days	Yes	Fecal-oral Droplet Contact	High	Low	Children Adults	Any	All	Worldwide
<i>Bacillus anthracis</i>	Anthrax	1 to 60 days	No	Aerosol Contact Ingestion	Moderate	High	All	Any	All	Worldwide, except Antarctica
<i>Blastomyces dermatitidis</i>	Blastomycosis	2 to 8 weeks	No	Inhalation	Low	Low	All	Any	Central/Midwest Southeast	Mexico Central America South America
<i>Bordetella pertussis</i>	Pertussis	5 to 21 days	Yes	Droplet	High	Low	Children Adults	Summer, Fall	All	Worldwide
<i>Chlamydia (Chlamydophila) psittaci</i>	Psittacosis	5 to 14 days	Rare	Inhalation Droplet	Low	Low	All	Any	All	Worldwide
<i>Chlamydia (Chlamydophila) pneumoniae</i>	Chlamydia pneumonia	1 to 4 weeks	Yes	Droplet	High	Low	All	Any	All	Worldwide
<i>Coccidioides immitis</i>	Coccidioidomycosis	1 to 3 weeks	No	Inhalation	High	Low	Adults	Any	Southwest Central/Midwest	Mexico Central America South America
Coronavirus	SARS	2 to 10 days	Yes	Droplet Contact	Low	Moderate	Adults	Any	All	Worldwide, except SARS-HCoV: China, Hong Kong, Taiwan, Singapore, Canada (last case 2004)
<i>Coxiella burnetii</i>	Q fever	2 to 3 weeks	Rare	Inhalation, Contact with contaminated materials, Tick bite	Moderate	Low	Adults	Any	All	Worldwide
<i>Francisella tularensis</i>	Tularemia	1 to 21 days	No	Aerosol Ingestion Animal bite Insect bite Aerosol Skin wound	Low	Moderate	All	Summer, Winter	All	Northern Hemisphere
Group A <i>Streptococcus</i>	Strep pharyngitis Rheumatic fever	1-3 days (strep pharyngitis)	Yes	Droplet	Moderate	Low	All	Winter, Spring	All	Worldwide
<i>Haemophilus influenzae</i>	H. influenza	Unknown	Yes	Droplet	Low	Low	Children Adults	Winter	All	Worldwide
Hantaviruses, New World	Hantavirus pulmonary syndrome	1 to 4 weeks	Rare (Andes virus)	Droplet, Aerosol, Mucous membrane	Low	High	Adults	Summer, Fall	All	North, Central, and South America
<i>Histoplasma capsulatum</i>	Histoplasmosis	3 to 21 days	No	Inhalation	Moderate	Low	Adults	Any	Central/Midwest	Worldwide, especially Central and South America

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Human metapneumovirus	Human metapneumovirus	2 to 8 days	Yes	Droplet Contact	High	Low	Children	Winter, Spring	All	Worldwide
Influenza viruses	Influenza	1 to 4 days (typically 2-3 days)	Yes	Primarily large droplet; likely small particle nuclei	Moderate to High	Depends upon affected population	All	Winter (U.S.)	All	Worldwide
<i>Legionella</i> spp.	Legionnaires' disease Pontiac fever	2 to 10 days, 1-3 days (Pontiac fever)	No	Aerosol Aspiration	Moderate	Moderate	Adults	Summer, Fall	All	Worldwide
<i>Mycobacterium tuberculosis</i>	Tuberculosis	2 to 10 weeks to positive tuberculin skin test (TST) (initial infection); Months or years to disease	Yes	Aerosol	Low	Low; May be moderate or high if drug resistant, especially if HIV co-infected	All	Any	All	Worldwide
<i>Mycoplasma pneumoniae</i>	Mycoplasma	2 to 4 weeks	Yes	Droplet	High	Low	Children Adults	Fall	All	Worldwide
Parainfluenza virus types 1-4	Parainfluenza	2 to 6 days	Yes	Droplet Contact Fomites	High	Low	Children	Fall (1,2) Spring (3) Summer (3)	All	Worldwide
Respiratory syncytial virus	RSV	2 to 8 days	Yes	Droplet Contact	High	Low	Children	Fall, Winter, Spring	All	Worldwide
Rhinovirus	Rhinovirus	2 to 7 days	Yes	Aerosol Droplet Contact Fomites	High	Low	All	Fall, Spring, Summer	All	Worldwide
<i>Streptococcus pneumoniae</i>	Pneumococcus	1 to 3 days	Yes	Droplet	Moderate	Moderate	Children Adults	Winter	All	Worldwide
<i>Yersinia pestis</i> (secondary to bubonic plague)	Bubonic plague with secondary pneumonic plague	1 to 7 days	Rare	Animal Contact Flea bite	Low	High	Children Adults	Spring, Summer	Southwest	South America Asia Africa
<i>Yersinia pestis</i> (primary pneumonic plague)	Primary pneumonic plague	1 to 6 days	Rare	Animal Contact Droplet	Moderate	High	All	Spring, Summer	Southwest	South America Asia Africa

**Differential diagnosis for a respiratory disease outbreak: Clinical information**

Pathogen	Predominant Respiratory Syndrome	Other associated syndromes or features (respiratory and non-respiratory)	Most common chest x-ray findings	Unique laboratory or pathology findings	Vaccine available in U.S.	Infection control precautions
Adenovirus	Pneumonia, Upper respiratory* Bronchiolitis, Croup, Pharyngitis	Conjunctivitis, Keratoconjunctivitis, Diarrhea, Rhinorrhea, Hemorrhagic cystitis, Disseminated disease	Patchy infiltrates	Smudge cells (pathology)	No	Standard, Droplet, Contact
<i>Bacillus anthracis</i>	Dyspnea associated with mediastinal changes, Pneumonia	Bacteremia, Meningitis, Gastrointestinal bleeding, Cutaneous lesions	Mediastinal widening, Large pleural effusions	Bloody pleural effusion	Anthrax Vaccine Adsorbed (AVA)	Standard
<i>Blastomyces dermatitidis</i>	Pneumonia	Febrile illness**, Cutaneous lesions, Hemoptysis, Weight loss Chest pain	Usually lobar or segmental consolidation; Chronic form mimics tuberculosis or sarcoid	Granulomatous lesions	No	Standard
<i>Bordetella pertussis</i>	Prolonged cough, Pneumonia	Apnea in infants, Rhinorrhea, Conjunctival involvement, Encephalopathy and seizures	Pulmonary consolidations in ~20-25% cases	Leukolymphocytosis	DTaP or TDaP (other combinations: DTaP-Hib, DTaP-Hepatis B-Inactivated polio)	Droplet
<i>Chlamydia (Chlamydophila) psittaci</i>	Pneumonia, Cough, Pharyngitis	Febrile illness**, Headache, Hepatosplenomegaly	Usually lobar consolidation; Chest radiograph often worse than clinical appearance	Mononuclear infiltrates, Intracytoplasmic inclusions	No	Standard
<i>Chlamydia (Chlamydophila) pneumoniae</i>	Pneumonia, Cough, Pharyngitis	Encephalitis, Sinusitis	Patchy infiltrates	Inclusion bodies (pathology)	No	Standard
<i>Coccidioides immitis</i>	Pneumonia, Cough	Weight loss, Arthralgias, Headache, Rash, Erythema nodosum	Unilateral infiltrates with adenopathy, Pulmonary nodules or cavities, Diffuse reticulonodular disease in immunocompromised	Neutrophilia and eosinophilia; Granulomatous lesions (pathology)	No	Standard
Coronavirus	Upper respiratory*, Pneumonia (SARS-HCoV)	Acute Respiratory Distress Syndrome (ARDS), Gastrointestinal involvement (SARS-HCoV)	Progressive infiltrates (SARS-HCoV)	N/A	No	Standard (all), Contact (HKU1, NL63, 0299E, OC43, SARS-HCoV) Airborne (SARS-HCoV)
<i>Coxiella burnetti</i>	Pneumonia	Febrile illness**, Headache, Sweats, Hepatitis, Endocarditis (subacute), Miscarriage	Variable appearance; May be rapidly progressive; Effusions in ~35% patients	Transaminitis	Yes	Standard
<i>Francisella tularensis</i>	Pneumonia, Pharyngitis	Indolent skin ulcer, Regional lymphadenopathy, ARDS, Abdominal pain, Diarrhea, Vomiting, Painful purulent conjunctivitis	Pneumonia often missed on chest radiograph; Variable findings including adenopathy and effusions	N/A	No	Standard
Group A <i>Streptococcus</i>	Pharyngitis, Pneumonia	Skin infections, Toxic shock syndrome, Necrotizing fasciitis, Bacteremia	Lobar consolidation	Elevated Antistreptolysin O Antibody (ASO) titer	No	Droplet
<i>Haemophilus influenzae</i>	Pneumonia	Meningitis, Bacteremia, Septic arthritis, Otitis media	Patchy or lobar infiltrates	N/A	Hib	Droplet
Hantaviruses, New World	Pneumonia, ARDS-like syndrome	Myalgias, Arthralgias, Nausea, Diarrhea, Cardiogenic shock	Asymmetric interstitial infiltrates, Pulmonary edema, Pleural effusions	Thrombocytopenia, Leukocytosis, Atypical lymphocytosis, Immunoblasts, Hemoconcentration	No	Standard
<i>Histoplasma capsulatum</i>	Pneumonia	Chest pain, Headache, Arthralgias, Weight loss, Hepatosplenomegaly, Erythema multiforme/Erythema nodosum, Pericarditis, Ocular choroiditis	Hilar adenopathy; Patchy infiltrates more common in lower lobes; Chronic form mimics tuberculosis	Granulomatous lesions (pathology)	No	Standard

\* Upper respiratory= nasal congestion, rhinorrhea, sore throat or bronchitis

\*\* Febrile illness= fever, myalgias, arthralgias, fatigue

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Human metapneumovirus	Pneumonia, Bronchiolitis, Upper respiratory*, Pharyngitis	Rhinorrhea	Diffuse interstitial infiltrates, Hyperinflation, Atelectasis	N/A	No	Standard and Contact
Influenza viruses	Upper respiratory*, Cough, Pneumonia	Febrile illness**, Myalgias, Croup, Bronchiolitis, Otitis Media, Sinusitis, Myositis, Myocarditis, Rhabdomyolysis, Encephalopathy/Encephalitis, Reye Syndrome, Exacerbation of chronic diseases	Variable	N/A	Inactivated split virus (IM), Live attenuated (intranasal)	Seasonal influenza: Standard and Droplet; Avian and Swine influenza: Standard, Contact, Droplet, Airborne
<i>Legionella</i> spp.	Pneumonia (Legionnaires' disease), Cough (Pontiac fever)	Febrile illness**, Diarrhea, Weakness	Interstitial infiltrates, Multilobar infiltrates; Pleural effusions	Hyponatremia; Acute fibropurulent pneumonitis in alveoli and bronchi (pathology)	No	Standard
<i>Mycobacterium tuberculosis</i>	Prolonged cough, Pneumonia	Lymphadenitis, Pleuritis, Hemoptysis, Meningitis, Weight loss, Osteomyelitis, Pericarditis, Genitourinary disease	Infiltrates with hilar adenopathy, Cavitory lesions, Miliary pattern	Positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) (does not distinguish disease from latent infection); Caseating or non-caseating granulomas (pathology); Positive smear for acid-fast bacilli; Diagnosis confirmed by isolation of <i>M. tuberculosis</i> from body fluid or tissue; Anemia uncommon	Bacille Calmette-Guerin (BCG); May be difficult to obtain as not routinely used in U.S.; Limited efficacy	Airborne
<i>Mycoplasma pneumoniae</i>	Pneumonia, Pharyngitis, Upper respiratory*	Erythema multiforme, Stevens-Johnson syndrome, Raynaud's phenomenon, Meningoencephalitis, Bullous myringitis	Variable	Cold agglutinins; Diffuse alveolar, hyaline membranes, pulmonary infarctions (pathology)	No	Droplet
Parainfluenza virus type 1-4	Pneumonia, Bronchiolitis, Upper respiratory*, Croup	Febrile illness**	Undescribed	N/A	No	Standard and Contact
Respiratory syncytial virus (RSV)	Pneumonia, Bronchiolitis, Upper respiratory*	Otitis media, Rhinorrhea, Sinusitis, Croup, Wheezing	Diffuse interstitial infiltrates; Hyperinflation; Atelectasis	N/A	No	Standard and Contact
Rhinovirus	Upper respiratory*, Pneumonia (high-risk groups)	Rhinorrhea, Asthma exacerbations, Chronic Obstructive Pulmonary Disease (COPD)	Undescribed	N/A	No	Contact
<i>Streptococcus pneumoniae</i>	Pneumonia	Sinusitis, Meningitis, Bacteremia, Otitis Media	Segmental or lobar pneumonia	Leukocytosis, Sputum may show gram-positive cocci	Conjugate (infant/children), Polysaccharide	Standard
<i>Yersinia pestis</i> (secondary to bubonic plague)	Pneumonia	Bubonic (fever and lymphadenopathy), Sepsis, Lymphadenopathy, Meningitis, Chest pain, Hemoptysis	Bronchopneumonia with patchy bilateral infiltrates	Sputum initially scant becoming blood-tinged and purulent with gram-negative bacilli; Characteristic morphology with Wayson or Wright-Giemsa stain; Leukocytosis; Gram-negative bacteremia	No	Droplet
<i>Yersinia pestis</i> (primary pneumonic plague)	Pneumonia	Sepsis, Disseminated Intravascular Coagulation (DIC), Chest pain, Hemoptysis	Dense lobar pneumonia which is usually unilateral with naturally occurring disease; Hilar lymphadenopathy	Sputum usually frothy, blood-tinged, purulent with gram-negative bacilli; Characteristic morphology with Wayson or Wright-Giemsa stain; Leukocytosis, Gram-negative bacteremia	No	Droplet

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Differential diagnosis for a respiratory disease outbreak: Risk factors for disease

Pathogen	Institutional clusters?	Specific group settings often affected	Occupation or avocation	Animal exposure risk factor	Environmental exposure	High risk activities	Persons with increased susceptibility or disease severity	Potential for bioterrorism agent?
Adenovirus	Yes	Day Care/School, Military Barracks, Dormitory	Military	None	Swimming pools, Ophthalmology offices		Infants, Post-transplant, Adults in crowded and stressful conditions	No
<i>Bacillus anthracis</i>	Yes	Occupational	Laboratory worker, Wool sorter, Drum maker, Animal handler	Infected livestock, Animal products from infected animal	Deceased animals, Aerosol (bioterrorism)	Processing of infected animal products		Yes
<i>Blastomyces dermatitidis</i>	No	None	Construction worker, Farmer	None	Soil, Dust clouds, Woods near water	Outdoor activity in mud or water	HIV, Post-transplant, Malignancy, Steroids	No
<i>Bordetella pertussis</i>	Yes	Day Care/School, Military Barracks, Dormitory	Healthcare worker	None	No		Unvaccinated communities	No
<i>Chlamydia (Chlamydomphila) psittaci</i>	No	None	Bird handler, Laboratory worker	Birds (especially psittacine)	Bird feces	Cleaning bird cages		No
<i>Chlamydia (Chlamydomphila) pneumoniae</i>	Yes	Day Care/School		None	No			No
<i>Coccidioides immitis</i>	Yes	Military	Farmer, Construction worker	None	Soil, Dust clouds	Excavation	HIV, Post-transplant, Filipinos, African-Americans	No
Coronavirus	Yes	None	Healthcare or Laboratory worker (SARS-HCoV)	None	No	Travel to affected areas (for SARS-HCoV infections)	Infants, Elderly, Diabetes mellitus	No
<i>Coxiella burnetii</i>	Yes	None	Animal handler, Laboratory worker	Primarily cattle, sheep, goats	Animal products of conception, Aerosol (bioterrorism), ticks	Occupational contact with animal or animal products	Pregnant, Immunocompromised, Existing cardiac valvulopathy	Yes
<i>Francisella tularensis</i>	No	None	Hunter, Animal handler, Landscaper, Farmer, Laboratory worker	Lagamorphs, Rodents, Ticks, Biting flies	Contaminated hay, mud or water	Mowing, Weed-wacking, Skinning, dressing, or eating game, Hunting, Outdoor activities	HIV (Typhoidal)	Yes
Group A <i>Streptococcus</i>	Yes	Day Care, Long-Term Care Facility/Nursing Home, Military	Military	None	No		Elderly, HIV, Diabetes, Skin breakdown, Malignancy	No
<i>Haemophilus influenzae</i>	Yes	Day Care/School		None	No		Asplenic, HIV, Sickle cell disease, Malignancy, American Indian/Alaska native children	No
Hantaviruses, New World	No	None	Construction worker, Grain farmer, Mammologist	Rodents	Rodent excreta	Outdoor activities, Cleaning/entering rodent-infested structures, Handling rodents		No
<i>Histoplasma capsulatum</i>	No	None	Construction worker, Spelunker	Bats, Birds	Soil enriched by bird guano, Bat guano	Excavation	HIV, Hematologic malignancies, Immunosuppressive medications	No
Human metapneumovirus	Yes	Long-Term Care Facility/Nursing Home		None	No		Infants, Children, Elderly	No

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Pathogen	Institutional clusters?	Specific group settings often affected	Occupation or avocation	Animal exposure risk factor	Environmental exposure	High risk activities	Persons with increased susceptibility or disease severity	Potential for bioterrorism agent?
Influenza viruses (Human influenza A, B, C viruses)	Yes	Day Care/School, Long-Term Care Facility/Nursing Home, Hospital ward/unit, Correctional facility/Shelter, Military Barracks/Dormitory, Cruise ship passengers		None	No		Children <5 years of age, Elderly, Persons with underlying diseases	No
Influenza viruses (Avian influenza A viruses, low and highly pathogenic)	No		Poultry workers, persons involved in poultry disposal operations	Sick or dead poultry; dead wild birds	Visiting a live poultry market	Direct unprotected contact with sick or dead birds; Close, prolonged unprotected contact with an ill human case	Unknown for most avian influenza A viruses; blood relatives of a human case of highly pathogenic avian influenza A (H5N1) virus infection	No
Influenza viruses (swine influenza A viruses)	No		Swine workers, swine veterinarians	Sick pigs				No
<i>Legionella</i> spp.	Yes	Travel Destinations, Healthcare settings		None	Aspirated potable water, Aerosolized water	Travel	Elderly, Chronic lung disease, Tobacco smoking, Post-transplant, HIV, Other immunosuppression	No
<i>Mycobacterium tuberculosis</i>	Yes	Correctional facility/Shelter	Healthcare worker	Airborne transmission from other mammals (very rare)	No	Living in homeless shelter, Incarceration, Participation in medical procedures (e.g., bronchoscopy) that generate aerosols	HIV, Post-transplant, TNF alpha blockade, Other immunosuppression, Homeless, Alcoholic, Incarcerated	No
<i>Mycoplasma pneumoniae</i>	Yes	Day Care/School, Long-Term Care Facility/Nursing Home, Prison/Shelter, Military Barracks/Dormitory		None	No		Asplenia, Sickle cell disease, Hemoglobinopathies, Hypogammaglobulinemia	No
Parainfluenza virus type 1-4	Yes	Day Care/School, Hospitals		None	No		Infants, Post-transplant	No
Respiratory syncytial virus	Yes	Day Care/School, Long-Term Care Facility/Nursing Home		None	No		Post-transplant, Malignancy, Chronic lung disease, Congenital heart disease, Premature infants, Elderly	No
Rhinovirus	Yes	Day Care/School, Long-Term Care Facility/Nursing Home		None	No		Post-transplant, Elderly	No
<i>Streptococcus pneumoniae</i>	Yes	Day Care/School, Long-Term Care Facility/Nursing Home, Correctional Facility/Shelter, Military Barracks/Dormitory	Military	None	No		Asplenia, HIV, Immunoglobulin deficiencies, Complement deficiencies, Chronic lung disease, Native Americans/Alaskans	No
<i>Yersinia pestis</i> (secondary to bubonic plague)	No	None	Hunter, Animal handler, Dog or cat owner	Fleas Rodents (rats, squirrels, prairie dogs) Pets with fleas	No	Outdoor activities Ingestion or handling contaminated tissues		No
<i>Yersinia pestis</i> (primary pneumonic plague)	No	None	Veterinarian, Cat owner, Healthcare or laboratory worker	Cats with pneumonic plague	Aerosol (bioterrorism)	Caring for plague-infected person or animal		Yes