

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-Hepatitis B-Inactivated polio)	Droplet
<i>Chlamydia (Chlamydia) 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 (Chlamydia) 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 burnetii</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

* Upper respiratory=nasal congestion, rhinorrhea, sore throat or bronchitis ** Febrile illness=fever, myalgias, arthralgias, fatigue

<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
<i>Human metapneumovirus</i>	Pneumonia, Bronchiolitis, Upper respiratory*, Pharyngitis	Rhinorrhea	Diffuse interstitial infiltrates, Hyperinflation, Atelectasis	N/A	No	Standard and Contact
<i>Influenza viruses</i>	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 spp.</i>	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
<i>Parainfluenza virus type 1-4</i>	Pneumonia, Bronchiolitis, Upper respiratory*, Croup	Febrile illness**	Undescribed	N/A	No	Standard and Contact
<i>Respiratory syncytial virus (RSV)</i>	Pneumonia, Bronchiolitis, Upper respiratory*	Otitis media, Rhinorrhea, Sinusitis, Croup, Wheezing	Diffuse interstitial infiltrates; Hyperinflation; Atelectasis	N/A	No	Standard and Contact
<i>Rhinovirus</i>	Upper respiratory*, Pneumonia (high-risk groups)	Rhinorrhea, Asthma exacerbations, Chronic Obstructive Pulmonary Disease (COPD)	Undescribed	N/A	No	Contact
<i>SARS CoV-2</i>	Upper respiratory*, Cough, Pneumonia	Acute Respiratory Distress Syndrome (ARDS), Pneumonia, Multisystem Inflammatory Syndrome (MIS), Guillain-Barre Syndrome, Post-Acute Coronavirus Syndrome	Consolidation, Reticular interstitial thickening, GGO	Increased CRP, ESR, IL-6, and LDH. Decreased Alb and Eos. Lymphopenia	Pfizer-BioNTech, Moderna, J&J/Janssen	Standard, Droplet, 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 (secondary to bubonic plague)</i>	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;	No	Droplet

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				Leukocytosis; Gram-negative bacteremia		
<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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