Influenza and Viral Pneumonia

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Hosted by Paul Webber
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Influenza and Viral Pneumonia

- Conflicts of interest
- Site investigator for a clinical trial investigating a new antiviral for adults with respiratory syncytial virus infection (Gilead)
- Site investigator for a clinical trial investigating a new drug for influenza (GlaxoSmithKline)

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- Objectives

- Review the epidemiology of the main respiratory viruses
- Highlight the difficulty to recognize a viral infection on clinical grounds
- Lay out a treatment strategy for patients with pneumonia and respiratory viral infection
- Point future directions

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- Outline
- Cases
- Epidemiology
- Clinical manifestations
- Treatment
- Future directions

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- Case 1
- A 65-year-old lady presents to the ER in January with the sudden onset of high temperatures, pleuritic chest pain and shortness of breath over the last 24 hours. She also has runny nose and malaise. She admitted having a household contact recently diagnosed with influenza. On physical examination, the patient appears ill and has a temperature of 39.9°C. A chest radiograph shows infiltrate in the right middle lobe. You diagnose the patient with community-acquired pneumonia and decide to admit her on the basis of vital signs and co-morbidities. You obtain blood and sputum cultures. A rapid influenza immunoassay sent by the triage staff member returns negative. What actions do you take?

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- Case 1

A. Start treatment for community acquired bacterial pneumonia with azithromycin only
B. Start treatment for community acquired bacterial pneumonia with ceftiaxone and azithromycin
C. Start treatment for community acquired bacterial pneumonia with antibiotics and for influenza with oseltamivir
D. Start treatment for community acquired bacterial pneumonia with antibiotics and for influenza with amantadine

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- Case 1

A. Start treatment for community acquired bacterial pneumonia with azithromycin only
B. Start treatment for community acquired bacterial pneumonia with ceftiaxone and azithromycin
C. Start treatment for community acquired bacterial pneumonia with antibiotics and for influenza with oseltamivir
D. Start treatment for community acquired bacterial pneumonia with antibiotics and for influenza with amantadine

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- Case 2
- A 41 year-old gentleman presents to the ER with cough, sputum production, pleuritic chest pain, and shortness of breath over the last 2 days. He had been diagnosed with influenza infection 3 weeks ago and received a treatment course with oseltamivir. On physical examination, his temperature is 39°C, respiratory rate is 28 breaths/min, blood pressure is 110/60 mmHg, and heart rate is 115 beats/min. On lung auscultation there are crackles on the right base. The CXR reveals an infiltrate in the right lower lobe. In addition to Streptococcus pneumoniae, which other pathogen would be of particular concern in this scenario:

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- Case 2

a) Klebsiella pneumoniae
b) Moraxella catarrhalis
c) Pseudomonas aeruginosa
d) Acinetobacter baumannii
e) Staphylococcus aureus

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- Case 2

a) Klebsiella pneumoniae
b) Moraxella catarrhalis
c) Pseudomonas aeruginosa
d) Acinetobacter baumannii
e) Staphylococcus aureus

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Epidemiology

- Respiratory viral infections are prevalent
- Affect vulnerable, such as children, elderly, and people living in developing areas
- Molecular techniques
- Pandemics and outbreaks

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Epidemiology

Pandemics and Outbreaks

- 1918 to 1919 Spanish influenza pandemic
- 1957 H2N2 Asian influenza pandemic
- 1968 H3N2 Hong Kong influenza pandemic
- 1977 H1N1 Russian influenza pandemic
- 2009 H1N1 pandemic
  - 201,200 respiratory deaths
  - 83,000 cardiovascular deaths
  - Most of these deaths occurred in patients younger than 65 years old

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Epidemiology

Pandemics and Outbreaks

- February 28 2013– Hospital contacted the Hanoi office of the WHO
- Patient presented with unusual influenza-like virus

Reilley B et al. N Engl J Med. 2003 May 15;348(20):1951-2.

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Epidemiology

Pandemics and Outbreaks

•Dr. Carlo Urbani answered the call
•He worked on the hospital, documented findings, arranged for samples to be tested

Reilley B et al. N Engl J Med. 2003 May 15;348(20):1951-2.

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Epidemiology

Pandemics and Outbreaks

- Of the first 60 patients with the illness, more than half were health care workers
- Many of the staff members made the difficult decision to quarantine themselves
- Some health care workers decided to sleep in the hospital

Reilley B et al. N Engl J Med. 2003 May 15;348(20):1951-2.

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Epidemiology

Pandemics and Outbreaks

- On March 9 2013 Dr. Urbani had a meeting with the Vice Minister of Health of Vietnam
- 4 four-hour discussion– the hospital was quarantined
- March 11, he began to have symptoms during a flight to Bangkok

Reilley B et al. N Engl J Med. 2003 May 15;348(20):1951-2.

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Epidemiology

Pandemics and Outbreaks

- 2003: Severe acute respiratory syndrome – Urbani strain of severe acute respiratory syndrome–associated coronavirus
- 2012: Middle East respiratory syndrome—coronavirus

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Epidemiology

Immunocompetent vs immunosuppressed

Community respiratory viruses

Endogenous reactivation
Community-acquired respiratory viruses

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Epidemiology

	Proportion of viral infection
Community-acquired pneumonia	24.5%
Hospital-acquired pneumonia	
Non-immunocompromised	11.2%
Immunocompromised	36.1%

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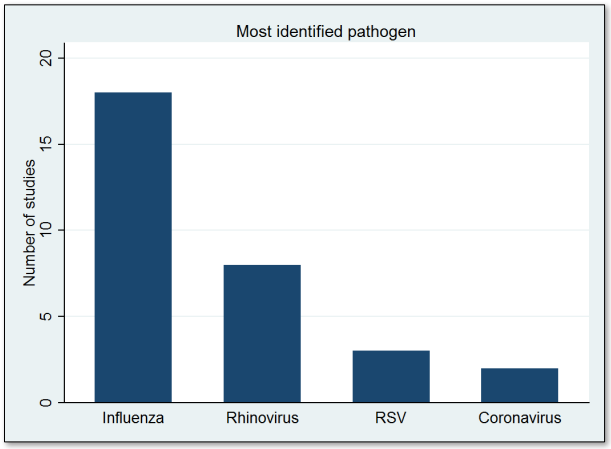
Epidemiology



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Epidemiology

Virus is a "bystander" and does not have a pathogenic effect.	Although uncommon in adults, asymptomatic carriage of respiratory viruses occurs.
Virus has a pathogenic effect and is causing pneumonia in isolation.	Potential mechanisms include dysregulation of cytokines and chemokines, infection of epithelial cells in the lungs, and apoptosis.
Virus has a pathogenic effect and is causing pneumonia along with a bacterial pathogen	A study showed that the mortality for patients with community-acquired pneumonia and bacterial and viral co-infection is higher.
Virus caused a recent infection that prompted a secondary bacterial infection.	This occurs particularly with *Streptococcus pneumoniae* or *Staphylococcus aureus* infection following influenza infection. Lag time of 2 to 4 weeks between the viral and bacterial infection. Polymerase chain reaction test may remain positive for up to 5 weeks after a viral infection.

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Epidemiology
Characteristics of the viruses

Table 1
Characteristics and taxonomy of commonly identified respiratory viruses in patients with community-acquired pneumonia

Virus	Genome	Family	Important Antigenic Structures
Influenza	RNA	Orthomyxoviridae	Surface glycoproteins hemagglutinin (HA) and the neuraminidase (NA).[8]
Respiratory syncytial virus	RNA	Paramyxoviridae	Attachment glycoprotein (G) and fusion (F) glycoprotein.[9]
Human rhinovirus	RNA	Picornaviridae	Viral capsid proteins VP1, VP2, VP3, and VP4.[10]
Adenovirus	DNA	Adenoviridae	Capsid major structures: hexon (the building block of the capsid), penton base, and polypetides.[11]
Parainfluenza	RNA	Paramyxoviridae	Surface glycoproteins hemagglutinin-neuraminidase and fusion protein. Membrane protein.[12]
Coronavirus	RNA	Coronaviridae	Membrane glycoprotein and spike protein.[13]
Human metapneumovirus	RNA	Paramyxoviridae	Virus fusion (F) glycoprotein.[14]
Human bocavirus	DNA	Parvoviridae	Capsid viral proteins (VPs), VP1, and VP2.[15]

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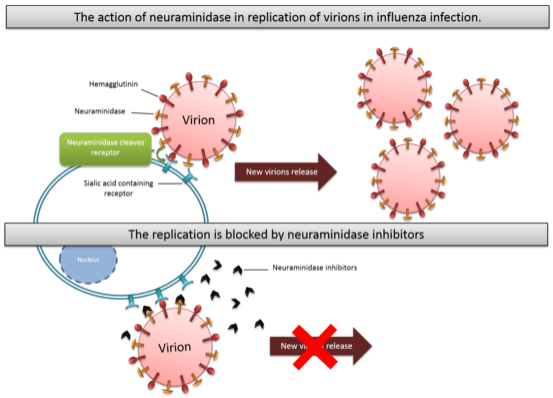
Epidemiology
Influenza



Available at: https://en.wikipedia.org/wiki/Discovery_and_development_of_neuraminidase_inhibitors

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Epidemiology
Influenza

- RNA virus
- Types A, B, and C based on its nucleoprotein and matrix protein
- Influenza A
  - H1N1, H1N2, and H3N2 based on hemagglutinin and neuraminidase
- Influenza B
  - B/Yamagata and the B/Victoria lineages

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Epidemiology
Influenza

- Antigenic drift: gene mutation that influenza undergoes every year
- Antigenic shift: new hemagglutinin or neuraminidase subtypes are acquired

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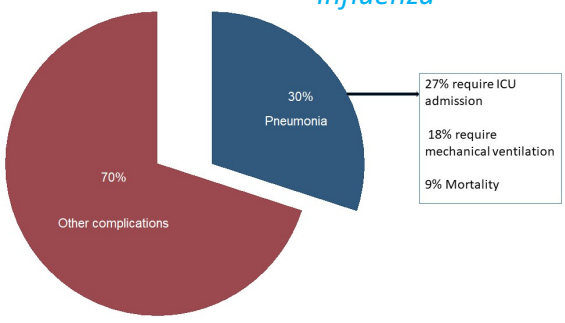
Epidemiology
Influenza



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Epidemiology
Respiratory Syncytial Virus

- In older subjects, the burden of RSV infection is similar to that of influenza
- RSV–associated hospitalization rate per 100,000 person-years
  - age 50 to 64 years: 12.8
  - > 65 years: 86.1
- Cohort of hospitalized patients > 65 years with RSV:
  - 31% had an infiltrate on chest radiograph
  - 15% required ICU admission
  - 13% required mechanical ventilation
  - 8% died

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Epidemiology
Rhinovirus

- Most common cause of common cold (2 to 4 times per year in adults)
- Sneezing, nasal discharge, sore throat, and low-grade fever
- Rhinovirus tends to occur more often in the early fall or spring
- Most commonly identified pathogen in a large cohort of adult patients hospitalized with community-acquired pneumonia conducted in the United States

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Epidemiology
Coronavirus

- Winter and follows seasonal pattern similar to influenza
- HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 are common cause of common cold
- Adult hospitalized patients with coronavirus infection are often immunocompromised, and pneumonia is a common
- Severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus

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Epidemiology
Adenovirus

- Common cause of upper respiratory tract symptoms and conjunctivitis
- Adult patients with adenovirus pneumonia are relatively young
- Causes serious infection in immunocompromised patients
- Outbreaks

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Epidemiology
Parainfluenza

- Most infections are caused by parainfluenza 1 and 3
- Influenzalike symptoms are a common manifestation of parainfluenza
- In children, common presentations are croup and bronchiolitis
- In hospitalized patients, age ranged 61.5 to 77.5 years
- Of those infected by parainfluenza-3, 59% had an infiltrate on chest radiograph

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Epidemiology
Metapneumovirus

- 4.5% of acute respiratory illnesses of adults prospectively followed as outpatients
- 4% of patients with community-acquired pneumonia
- Mean age in CAP and metapneumovirus infection: 62 years

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Epidemiology
Human bocavirus

- More common in children
- More common in the winter
- Common clinical presentations include upper respiratory tract symptoms, bronchiolitis, and pneumonia
- Detected in acute respiratory illness of adults with immunosuppression and chronic lung disease

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Clinical Manifestations
Influenza

- Cough
- Fever
- Fatigue
- Myalgia
- Runny nose
- Wheezing
- Dyspnea

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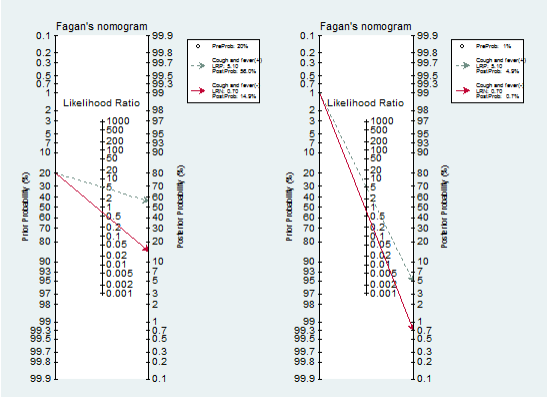
Clinical Manifestations

Influenza



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Clinical Manifestations

Influenza

- Symptoms or clinical impression are not enough to rule in or rule out influenza
- Clinicians failed to clinically diagnose influenza in approximately two-thirds of influenza-confirmed patients
- Surveillance data
- Contact with persons with acute febrile illness
- Recent travel

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Clinical Manifestations
Respiratory Syncytial Virus

- Wheezing
- Clinical-radiological dissociation
- Cough (97%)
- Dyspnea (95%)
- Wheezing (73%)
- Physical examination
  - Wheezing (82%)
  - Temp > 39°C (13%)

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Clinical Manifestations
Other Viruses

- No specific clinical manifestations
- Diagnosis of viral infection in patients with pneumonia relies on the recognition that respiratory viruses are a common etiology

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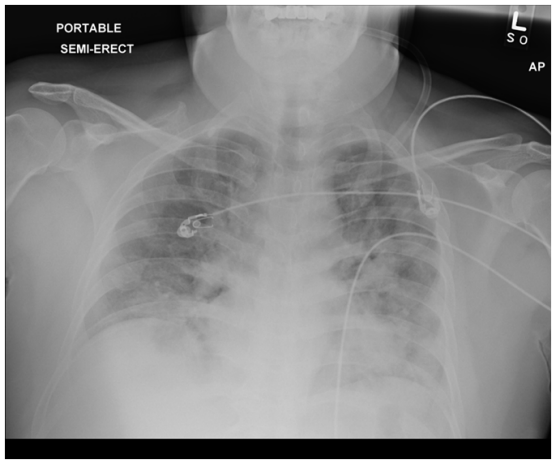
Radiological Manifestations



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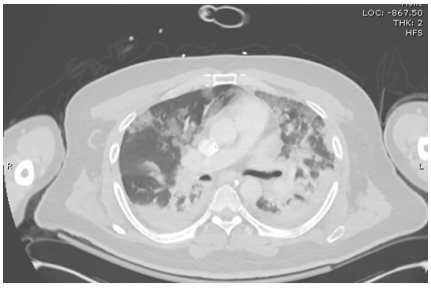
Radiological Manifestations



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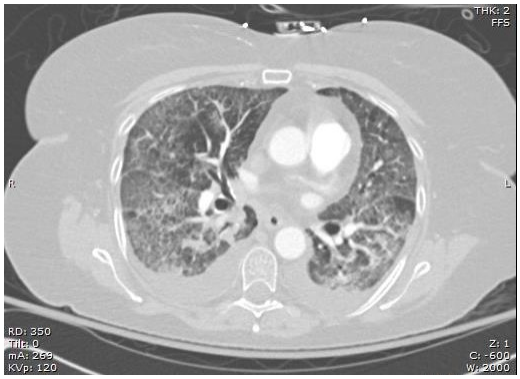
Radiological Manifestations



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Treatment

Approach to the patient with community-acquired pneumonia

Empirical treatment for influenza

- Point-of-care PCR available
- Influenza season

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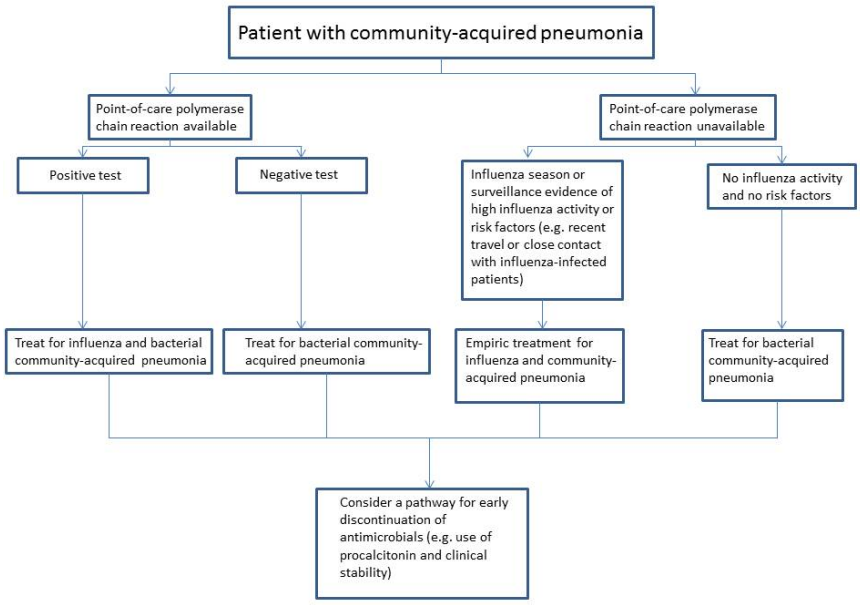

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Treatment

Viral pathogen-directed therapy

- Immunocompetent vs Immunosuppressed
- Risk factors (e.g. pregnancy)
- Severity of illness

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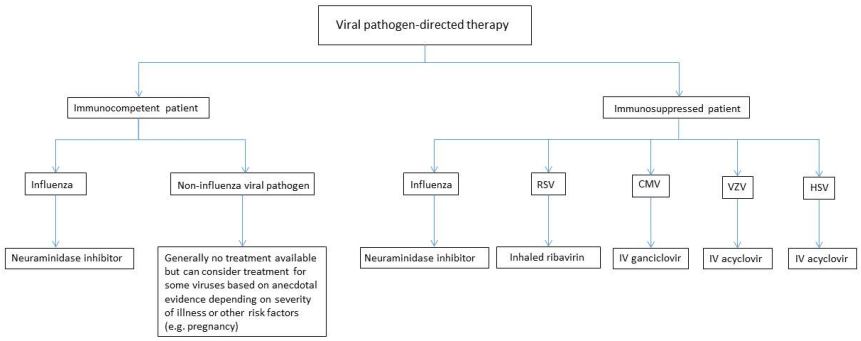
Treatment

Viral pathogen-directed therapy



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Treatment

Viral pathogen-directed therapy

Influenza

Alleviation of symptoms	8 studies	2208 patients oseltamivir 1746 patients in placebo	16.8 hours; 95% CI 8.4–25.1 hours
Pneumonia prevention	8 studies	2694 patients oseltamivir 1758 in the placebo group	Risk difference of 1% [0.22%–1.49%]
Hospitalization prevention	7 studies	2663 patients oseltamivir 1731 in the placebo group	Risk ratio 0.92; 95% CI 0.57–1.5

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Treatment

Viral pathogen-directed therapy

Influenza

- Hospitalized
- Severe, complicated, or progressive disease
- Higher risk for influenza complications

- Benefit greatest when it is started early
- Survival benefit has been demonstrated with treatment up to 5 days after symptom initiation

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Discontinuation of Antibiotics

- Clinical pathway
  - Viral microbiology testing plus procalcitonin

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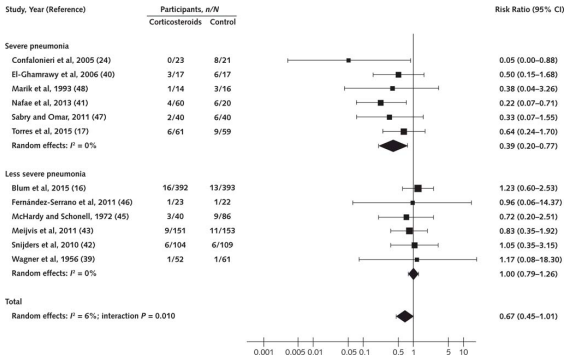
Corticosteroid therapy



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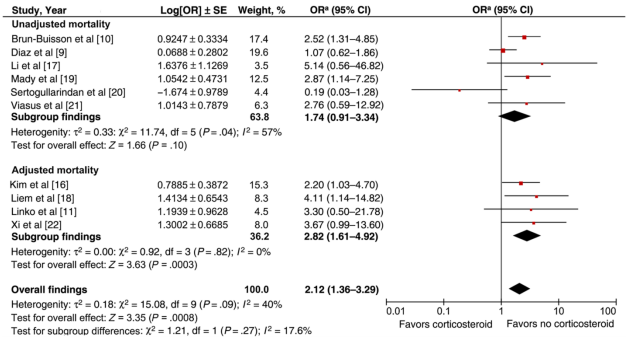
Corticosteroid Therapy



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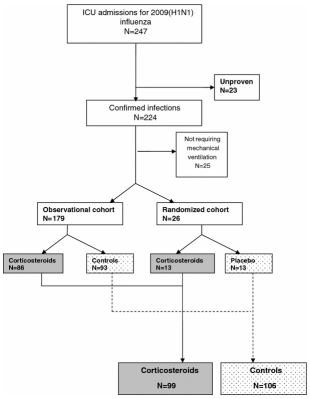
Corticosteroid Therapy



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Future Research

- Clinical pathways using point-of-care tests
- New antivirals
  - Fusion inhibitor for RSV
  - Inhibition of mRNA synthesis for influenza
- Combination therapy for influenza and other viruses

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Take-home points

- Respiratory viral infections are common
- 25% of patients with community-acquired pneumonia
- Also common in hospital-acquired pneumonia
- Outbreaks and pandemics
- Immunocompetent vs Immunosuppressed
- It is difficult to diagnose influenza or other viral infection on clinical grounds

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Take-home points

- PCR based tests
- Pathogen directed therapy
  - Immune status
  - Risk factors
  - Severity of illness

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THANK YOU

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March 26, 2019	*(European Teleclass)* **TAMING THE BUGS: CONTAMINATION AND INNOVATIVE APPROACHES TO STETHOSCOPE DISINFECTION** Speaker: **Prof. Gabriele Messina**, University of Siena, Italy
April 3, 2019	*(South Pacific Teleclass)* **HEALTHCARE ASSOCIATED INFECTION SURVEILLANCE IN THE ERA OF ELECTRONIC HEALTH DATA** Speaker: **Prof. Phil Russo**, Deakin University, Australia
April 9, 2019	*(FREE European Teleclass … Denver Russell Memorial Teleclass Lecture)* **MODERN TOOLS FOR BACTERIAL IDENTIFICATION AND ANTIBIOTIC SUSCEPTIBILITY TESTING** Speaker: **Prof. Vincent Cattoir**, Université de Caen Basse-Normandie, France
April 18, 2019	**INFECTION CONTROL ISSUES IN HEALTHCARE CONSTRUCTION, PART 1 - RENOVATION** Speaker: **Andrew Streifel**, University of Minnesota
May 2, 2019	*(FREE Teleclass)* **MEAT, MONKEYS, AND MOSQUITOES: A ONE HEALTH PERSPECTIVE ON EMERGING DISEASES** Speaker: **Prof. Laura Kahn**, Woodrow Wilson School of Public and International Affairs, Princeton University


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